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DERMATOLOGY IN A CHANGING WORLD*

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This, the fifty-fourth session of the American Dermatological Association, finds us assembled farther north than we have been since 1895, when the meeting was held in Montreal. Probably there are few, if any, here today who attended that gathering, so that we are all experiencing for the first time the spirit and hospitality of our Canadian comrades. Having seen something of the charm and beauty of the city, I can fully understand the reason for the cordial invitations given by Dr. King-Smith. No wonder he wants to share these good things with us, and I can say with the Psalmist, "Our lot is cast in pleasant places."

We are now an incorporated body. All legal matters necessary for the change have been completed and the name of our organization is now secure, together with the benefits for which this step was taken. The Association can receive property by gift or legacy, to be used in research or for promoting the general welfare of dermatology and syphilology according to the wishes of the donor or the discretion and judgment of our board of directors.

Research may well include the seeking of new and better remedies or drugs for the relief or control of dermatologic conditions, as well as the study of the cause and nature of the disease itself. The quality of work done by Schamberg, Cole, Stokes and others in the production, perfection and clinical application of drugs and methods of use clearly indicates that we have the ability and training to carry on such investigations.

We have seen great progress in recent years in the treatment for syphilis through the introduction of new drugs and methods of administration, as well as the application of nonspecific therapy. Hospitalization for malarial inoculations and the technical requirements for intraspinous and, in some cases, even intravenous injections require skill that tends to limit their general adoption in private practice.

Is it beyond hope that further study of some of the drugs of proved worth like bismuth may find a wider use in general through

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the production of a preparation that retains its efficiency when given by mouth?

Further study may reveal the part fever plays in Nature's defense mechanism against infections in general and *Spirochaeta pallida* in particular, as well as the safest and most effective method of raising the temperature of the body artificially, whether by electrical apparatus, injections of nonspecific protein, malarial inoculations or, perhaps, something even better; also their practical value, if any exists, in the early stages of syphilis. Safe and simple means assure a wide field of application and usefulness.

There is as yet no adequate medical, social or public health control of syphilis. Can the Association, working by itself or in cooperation with public health agencies or national societies, help to reduce the multiform effects of this far-reaching disease? Syphilis has always shown an increased occurrence in times of war and of social and economic unrest or depression. The present year is apparently no exception.

Reports from abroad indicate that our country is falling behind many, if not most, of the European nations in decreasing the incidence of syphilitic infections. If this is true, can our organization suggest the remedy? Being country-wide, it is familiar with local conditions and the means of control best suited to the needs of a given section.

From the medical point of view, prompt and thorough treatment in all infectious cases, applied as early as possible, is the effective means of control. Treatment is often a serious item of expense to the patient, in both time and money. The loss of wages while attending the clinic was practically the same as the cost of medication in one of our study groups at the Massachusetts General Hospital some time ago.

This expense of medical care is often given as an important underlying factor in the lack of thorough treatment for syphilis. In certain countries this situation is met by the Government's assuming the cost of management and treatment of venereal diseases. Such a procedure would not be feasible in the United States. Should this responsibility be assumed by the various states?

The medical profession generally dislikes the suggestion of state medicine. However, the state of Massachusetts spends $200,000 a year for the care of patients with dementia paralytica alone in state institutions. With this burden, it is only natural that the state should consider trying to eliminate this expense in human life and property by assuming control of early infections as it safeguards the source of its water supply.

Lay organizations have demonstrated that syphilis can be treated throughout at moderate fees, with a balance remaining after paying the staff and all necessary overhead expenses. Institutions of this kind

should be controlled by the medical profession rather than by laymen, and any profit accruing should go to an organization rather than to individuals.

The poor and the well-to-do are fairly well provided for at present. The burden of sickness falls heaviest on the persons in moderate circumstances.

Among the useful means of limiting the spread of infectious diseases, medical education holds an important place, and the responsibility of adequate medical instruction rests squarely on the medical schools.

During the past ten or fifteen years, the time allotted for teaching dermatology and syphilis has been definitely shortened in some of our grade A schools; e. g., Harvard now gives five hours of lectures and twenty-two hours of section work for the two subjects during the third year, whereas a decade ago each subject had sixteen hours of lectures and thirty-six hours of section work.

There is still a definite need of thorough knowledge of the natural history and clinical manifestations of syphilis. The diagnosis of early syphilis should not be difficult at present for the properly trained physician, and the value of such diagnosis as a basis for immediate treatment needs no comment. Recently a man with late syphilis said that he was left without medication for six months, awaiting a positive diagnosis of his primary syphilis—a condition that still occurs far too often. Can adequate treatment be expected to follow such delay?

Education of the public may have little effect in restraining venereal exposure, but it should be of service in bringing infected persons promptly under medical care.

Whether or not we realize it, times and manners are changing in medicine, as well as in business, industry and religion. It is as impossible for the dermatologist to escape contact with modern business at it would be to practice his specialty equipped only with clinical experience and a prescription pad.

> "New occasions teach new duties;
> Time makes ancient good uncouth.
> They must upward still and onward
> Who would keep abreast of truth."

To do so in this age of change, we must take heed of the situation, and, after careful consideration, determine our course and policy, retaining as far as possible all that is good in our traditions and principles.

Better business bureaus have been formed in many cities for the purpose of putting business on a higher, cleaner and more ethical basis. They are seeking outside help and constructive criticism in the matter of advertising. What shall be out attitude and policy

toward this phase of modern business in matters pertaining to our special field in medicine? Many of the drugs in daily use were given to hospitals and physicians for a thorough clinical trial and approval before being placed on sale. Arsphenamine is a notable example. Is this a condition worthy the consideration of the Association?

Another phase or contact with business and industry has arisen as a consequence of workmen's compensation insurance, some form of which has been adopted by the United States Government, its insular possessions and forty-four of the forty-eight states in the Union. The dermatologist may be brought into this field of industrial medicine either as the workman's physician, as the physician for an insurance company or as an impartial examiner appointed by the accident board to help in their decisions.

Industrial dermatoses form an important and increasing, if not a large group of industrial accidents. In 1912, Herxheimer listed seventy-four trades which he called provocative of "eczema dermatitis." Estimates of the frequency of industrial dermatoses in general skin clinics vary widely: from the 2 per cent reported by Fordyce to as high as 20 per cent, as given by Hazen and others. The percentage naturally increases in clinics located near manufacturing centers. During the war there were many industrial dermatoses among the workers in munition plants. These have disappeared, except where the offending chemicals have found their way into industrial processes.

Chemistry is being called on more and more by manufacturers to help meet competition in the costs of production, either by the substitution of cheaper materials or by chemical treatment which shortens the time or process of manufacture—either of which may increase the industrial hazard.

Until recently dermatomycoses were found chiefly among preparatory school and college students (usually athletes), golfers and other sportsmen, and for them consitituted a real recreational hazard not often seen among the working classes.

In both England and Germany, I believe, mycotic infections are not considered as industrial accidents. The accident board in Massachusetts takes a more liberal view, and considers certain of these cases compensatable. Wool and leather are credited by White as sources of epidermophytosis, and workers in flour, starch, rattan canes, etc., have been reported as suffering from occupational yeast and fungus infections.

Our board regards as compensatable certain cases of industrial dermatitis which subsequently become complicated with fungus infection. Such contamination often greatly prolongs the workman's incapacity.

Without attempting a complete list and omitting details, I shall cite some of the changes that affect dermatology directly or indirectly:

1. Group medicine: This includes either medical or surgical clinics.

2. State medicine: At present, without using that name, state and city boards of health are encroaching more and more on our special field in the supervision and treatment of tuberculosis, syphilis and cancer.

3. Institutes for the treatment of venereal diseases have been organized by laymen and are run by a paid medical staff on a purely business basis.

4. Various "institutes" and "systems" are run on similar lines, and prey on the vanity of those with lost or misplaced hair and other dermatologic defects, conditions and diseases.

5. The establishment of "tumor clinics" in general or special hospitals furnishes another group contact for dermatologists.

6. The development of physical therapy, particularly light treatment, has made changes in our special field. It is apparently not without disadvantages, seemingly having had a stimulating effect on the kind and number of suits for malpractice, which is directly reflected in high rates of liability insurance for those who use x-rays, ultraviolet light, etc.

It is unnecessary to mention further instances or to allude to the general commercial tendencies that are finding their way into medical practice, both general and special. This is largely due to the natural readjustments in medical practice required if our profession is to assume and maintain its proper position in the changing world.

This topic is not presented either in the light of a discovery or as a report of all the changes that are taking place about us. It seems timely that the subject should be presented in the hope of some time receiving the consideration of a large and important society.

Sooner or later some of us will be called on for individual action under some of these changed or changing conditions. If the consensus of this organization regarding these matters is known, we shall be in a position to govern ourselves according to the high standards and ideals of the Association.

TRYPARSAMIDE THERAPY

A FOLLOW-UP REPORT ON SEVENTY-SIX PATIENTS WITH NEUROSYPHILIS TREATED WITH TRYPARSAMIDE *

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Ten years have passed since tryparsamide was given to Lorenz and his colleagues by the Rockefeller Institute to be tried clinically for patients suffering from various forms of syphilis. Six years have passed since it was put on the market for general use by Merck and Company. Ten years are sufficient for a survey of the value of a drug, for one can discuss both its immediate and continued results.

LITERATURE

In a review of the literature, it was interesting to note how little has been written about tryparsamide in comparison to the vast amount written about malarial therapy, which was first tried in 1922. If the literature were any indication of the extent of its usage, I should feel that tryparsamide is still a relatively unknown drug.

A complete bibliography will be found at the end of this paper. On glancing over it, one realizes that in Europe tryparsamide is practically unknown. The only French article I could find is by Guillain and Girot,[3] 1924, in which the authors report the use of four, ten and twelve doses of tryparsamide, respectively, in three patients with dementia paralytica. The patients showed no improvement, and the authors concluded, therefore, that the drug is useless. The German reviews on the modern treatment of neurosyphilis do not even mention tryparsamide. Outside of the United States, South Africa is the only place where it has been tried and is still being used, and comprehensive reports have come from there.[22] Encouraged, perhaps, by these, there have been reports from two clinics in London (references 23 and 24).

Tryparsamide has also been relatively little discussed in and about New York. It was condemned by Fordyce and Myers in July, 1923,[7] in an article which dealt mainly with the arsenical penetration of tryparsamide into the spinal fluid of patients. It was tried on a few

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patients suffering from late symptoms of neurosyphilis, but since it did not cure them, its value was questioned. Another article coming from New York City is by Hecht [25] who bases his statements on ten patients treated at Montefiore Hospital without improvement. He does not mention the types or the stages of the disease, or the amount or number of treatments given, but he concludes, emphatically, that the drug should not be administered. A third article, by Kennedy and Davis,[9] treats of the value of the drug in detail. The authors base their report on thirty-one cases. However, the most comprehensive survey of the drug comes from several reports by Lorenz and his co-workers, Cady and his co-workers, Stokes and the group at the Mayo Clinic that carried on his work after he left, and by Stokes himself, and numerous reports in the *United States Veteran Bureau Medical Bulletin* (references 1; 11, 15, 18, 20, 27, 32, 40, 48 and 49), by various physicians working in the government clinics in different parts of the country. These reports are of paramount importance because they cover a number of years.

At first, many of the reports, except those by Lorenz and Cady (references 1 and 18), showed great skepticism of the value of tryparsamide over other drugs, pointing out the grave danger to the optic nerve from this form of arsenic. However, subsequent reports by the same men show that in many cases the patients had been given insufficient amounts and that they afterward began to improve when given more injections of the same drug. The workers found also that if the dosage was more carefully graded, the interval of time between injections increased to a week or ten days and a rest period of two months instead of one allowed between courses, then tryparsamide was no more injurious to the optic nerve than any other form of arsenic.

In May, 1925, Stokes and Wilhelm [15] reported on 152 cases at the Mayo Clinic in which tryparsamide was used. At that time, they found improvement in 47 per cent of all cases in which tryparsamide had been used, as compared with 62.8 per cent improvement found by Lorenz [1] and 66.6 per cent found by Moore.[5] In this series, they reported reactions in the eyes in 8 per cent of the patients—2.6 per cent with organic ocular changes and 5.4 per cent without them.

In 1926, O'Leary and Becker published further observations on these cases,[21] but they eliminated forty advanced paretic cases taken from the State Insane Asylum, and added seventy-five which had been under observation since 1924. Most of the patients had been given at least twenty injections of tryparsamide. They reported that: 1. In paretic patients (early in type) there was marked improvement in 12 per cent, improvement in 66 per cent, and no improvement or progression in only 22 per cent. (The normal spontaneous remission in early paresis is

11 per cent.) 2. In tabetic patients there was improvement in 9, or 39 per cent, and no improvement in 14, or 51 per cent. 3. In seventeen unclassified cases of neurosyphilis, there was marked improvement in 7 patients, or 41 per cent. 4. In six congenital syphilitic patients (five of whom were paretic and 1 tabetic), there was improvement (clinically) in two, or 33 per cent, and improvement (serologically) in two, or 33 per cent, although these showed little clinical improvement.

As compared to the ocular complications in 8 per cent of the patients in the previous report, only 5 patients of 207, or 2.4 per cent, had ocular disturbances during treatment, and of these 5, 3 were tabetic, a type of syphilis in which optic atrophy is a frequent and natural complication as the disease progresses. Three courses of tryparsamide were given to 3 other patients with optic atrophy without causing any change in the condition of their eyes, and in 3 cases the general condition of the patients improved.

The authors further discovered that when ocular disturbances occur, they do so at about the fourth injection of the first series. At this time, not enough of the drug has been given to cause permanent injury.

A follow-up report on the late results of treatment with tryparsamide was published on April 21, 1928, by Lorenz and his workers.[35] Of 317 patients suffering from dementia paralytica who were treated with tryparsamide, 152 reported to him. Of these, 134 remained well for from five to six years, 4 died, and 14 returned to the State Hospital. The authors found that the expansive type responded the best. Even in those showing less improvement, however, the general condition improved, and in almost all cases, there was an increase in body weight and strength. They also found that the serology changed most frequently in the patients showing improvement, although there was no change which could act as an index of improvement. Thus the colloidal gold curve, having a paretic curve, would tend to approach a meningitic curve, and the cells in the spinal fluid would tend to decrease. They furthermore found that improvement could not be despaired of until 150 Gm. of tryparsamide had been given.

All the more detailed reports on treatment with tryparsamide show improvement in a large percentage of patients with early cases of paresis, with meningovascular syphilis and with latent paresis demonstrating few symptoms but a positive serology. In the old, broken-down patients with paresis, little improvement was obtained. In the reports of Henderson,[32] 1928, and of Fong,[31] 1928, a comparison is made between treatment with malaria and with tryparsamide. In the early cases of neurosyphilis, the results are about the same. They found that the advantages of tryparsamide over malaria are that the former can be given without hospitalizing the patient, and that the patient need not

be unusually healthy for this type of therapy to be tried. Hence, it is available to patients, 50 or 60 years old, for whom malarial therapy would not be advocated.

In reviewing the literature, I found that tryparsamide had been used relatively less in tabes dorsalis than in other forms of neurosyphilis. It may be that a larger number of patients suffering from paresis were found in the clinics, or that the investigators were more eager to find a cure for paresis because of its graver social aspect. In analyzing our cases, therefore, I was more than pleased to find that a large percentage were of tabes dorsalis. I believe that this report is important so far as it analyzes the value of tryparsamide in the treatment for tabes dorsalis.

RESULTS OF TRYPARSAMIDE THERAPY

The report presented in the following pages is an analysis of seventy-six patients treated with tryparsamide at Cornell Clinic since 1925. They had received no form of treatment for the past one to three years, but returned to the syphilitic department for follow-up every six months to one year. No patients have been included who are still under treatment or who have had treatment since December, 1929.

All of the patients had had some form of antisyphilitic treatment prior to that with tryparsamide. In most of the cases tryparsamide was combined with bismuth which was administered intramuscularly. Since tryparsamide has almost no spirochetocidal value, my associates and I felt that it was safer to give some antispirochetal therapy simultaneously with tryparsamide.

All of our patients were ambulatory, which may explain the large number of patients with tabes dorsalis.

I have divided the patients into five groups: those with paresis and taboparesis, 11; with tabes, 41; with meningovascular syphilis, 15; with early syphilis of the central nervous system, 8, and those with congenital syphilis, 1. Moreover, I have separated the male patients from the female patients to determine whether or not there exists a difference in the therapeutic value of tryparsamide for the two sexes.

Paresis and Taboparesis.—Among the eleven paretic and taboparetic patients, there was one woman and ten men.

The one woman was 39 years old. She had had the disease over ten years before any treatment was begun. She had had eight injections of arsphenamine and six of mercury before tryparsamide was tried. She had an early but full blown expansive type of paresis, coupled with marked depressions and insomnia. She received twenty-five injections of tryparsamide over a period of eighteen months. The Wassermann reaction, which had been 4 +, became negative. The spinal fluid, which had shown a 4 + Wassermann reaction and a typical

paretic curve, also became negative. The symptoms disappeared and her general condition improved to such an extent that she could resume her usual activities. There has been no relapse in two years.

The average age of the ten men was 43. The average duration of the disease before any treatment was begun was twenty years. Five patients did not know how long they had had the infection. One patient was treated irregularly for one year after the onset of the disease and then received no treatment for fifteen years. There were six late cases of paresis, a stage in which institutions would have been the proper place, but the families of the patients preferred to shield them. There were four early cases, in which, however, the symptoms were full blown.

These ten men had had an average of seventeen injections of arsphenamine. Six had not received arsphenamine. They had had an average of twenty-six injections of mercury, while six had not received mercury. They had had an average of twenty injections of bismuth. Four had received no bismuth prior to the treatment with tryparsamide. One patient had taken mercury by mouth for one year.

The average number of injections of tryparsamide to a patient was twenty-five. The largest number of injections given one patient was forty. Six of the ten showed marked improvement. Two of these were late cases, and four early cases. Two patients with late cases showed improvement, one remained stationary, and one became worse.

We found the same discrepancies between the symptomatology, physical signs and serology that have been reported by all previous writers. Thus: three Wassermann reactions became negative; two became decreased; three remained the same: one negative, one 4 + and one ±, and two became increased: one rose from 2 to 4 + and the other rose from ± to 2 +.

Similarly, there were marked variations in the spinal fluid. We performed six examinations of the spinal fluid in this group, before and after treatment with tryparsamide:

Two Wassermann reactions remained unchanged, but the colloidal gold curve became meningitic in type. (The patients showed marked improvement.) Two Wassermann reactions remained negative. The colloidal gold curve became negative, and the patients showed no improvement. One Wassermann reaction became negative, the colloidal gold curve became meningitic in type, and the patient improved. One Wassermann reaction became 2 +, the colloidal gold curve remained 555544300, and this patient showed a most marked improvement and has been well and carrying on his former occupation as a mechanic without interruption for two and a half years.

Thus, in this group of eleven patients, 81 per cent are improved, 63 per cent of them markedly so.

The group is relatively small and therefore conclusive deductions must not be drawn from it. However, the percentage figures agree with those of Lorenz, Cady, Stokes and O'Leary in their reports on a large number of paretic patients (references 35, 49, 15, 36, 21 and 51, respectively).

Meningovascular Syphilis.—Among the fifteen patients suffering from a meningovascular form of syphilis, there were three women and twelve men.

The average age of the women was 38. The average duration of the disease before any form of treatment was instituted was two and a half months. One of the three women did not know how long she had had the infection. This patient had received neither arsphenamine nor bismuth, but had had sixteen injections of sulpharsphenamine before coming to the clinic. Because of her marked generalized meningitic symptoms—headache, deafness (sudden in onset) and severe dizziness—tryparsamide was tried immediately. She was given fifty-two injections in all, as well as injections of bismuth during the course, and in the intervals, mercury rubs. Her condition cleared up completely after a month, and she has remained well for one year. To the other two women, an average of thirteen injections of arsphenamine, thirty-seven of mercury and thirty-one of bismuth had been given. One of these patients had also had twelve injections of sulpharsphenamine. The average number of injections of tryparsamide were twenty-seven. Two patients improved markedly. One patient improved, though some of the symptoms remained. In two of the patients, the Wassermann reaction became negative, and in the other, it became 1 +. Only one examination of the spinal fluid was made. The Wassermann reaction which was 3 + became negative and the colloidal gold, which had had a typical meningitic curve, 123321000, became negative.

The average age of the twelve men was 43 years, and the average duration of the disease before any treatment was begun, eight years. In three of the patients the duration could not be elicited.

The average number of injections of arsphenamine for this group was 18. One patient had had 75 injections. The average number of injections of mercury was 34. One patient received 100 injections. The average number of injections of bismuth was 31; the largest number to a single patient, 96. The average number of injections of tryparsamide was 27. One patient received 68 injections. When, however, this patient showed no improvement after the fifty-third injection, the bismuth was discontinued and only tryparsamide given; he improved greatly. He subsequently was given two more courses of tryparsamide, and made an excellent recovery.

Seven patients in this group showed a marked improvement, two improved, and three showed no improvement. When the men and women are grouped it is found that 80 per cent of the patients improved clinically. In this group, as in the previous one, the number of cases is too small to draw far-sweeping deductions.

Cerebrospinal Syphilis.—There were only eight patients suffering from early forms of cerebrospinal syphilis. This type of the disease is a transitional one. It has few symptoms, and so is listed in the reports of many authors as latent paresis, tabes or meningovascular syphilis. This group includes patients with fixed pupils and a positive serology but no symptoms, or patients with a positive history of syphilis, increasing nervousness and hyperactive reflexes, at times with a positive or negative serology. I do not believe that the disease in these patients should be classified as latent, but this prejudice may arise from a purely personal impression of the patients. The average duration of the disease in this group before any treatment was begun was twenty months. An average of twenty-one injections of arsphenamine had been given, thirty-three of mercury and thirty of bismuth. The average number of injections of tryparsamide in this group was seventeen, the largest number twenty-four. Four patients, or 50 per cent, became markedly improved, two, or 25 per cent, became improved, and two, or 25 per cent, became worse. In this group, our percentage of improvement is less than that obtained by other reporters.

Congenital Syphilis.—A girl, 7 years old, with ocular signs and mental deficiency, who had been treated since birth, was given twenty-four injections of tryparsamide. She improved during the first course, became alert, less irritable and was able to go to school; she has improved since then, although she has been without treatment for one year. Her mentality is still about two years subnormal, but she seems to be developing into a useful, social human being. Her eyes have improved in spite of the injections of tryparsamide.

We have under treatment at present, a boy of 17 with similar symptoms who is improving, but as he has not completed his treatments, he does not come into the scope of this paper.

Tabes Dorsalis.—We have treated forty-one patients with tabes dorsalis—seven women and thirty-four men—twenty-six of whom presented late cases—five women and twenty-one men.

The average age of the seven women was 36 years; the average duration of the disease before any treatment was taken, three years. Four patients did not know the duration of the infection. Three patients began treatments three months after the onset of the disease, and one patient began ten years after the first manifestation.

The average number of injections of arsphenamine in this group of women was eighteen. Three patients had had no arsphenamine. The average number of injections of mercury was twenty-four; one patient had had eighty-one injections, and one had had no mercury. The average number of injections of bismuth was forty-two. One patient had had eighty-two injections, and two had had none. The average number of injections of tryparsamide was fifteen, the largest number administered was thirty-six, the smallest, five.

The patient who received only five injections of tryparsamide had some blurring of vision; therefore, we stopped giving her tryparsamide. She had been feeling a little better, however, even after four injections. Today, we have had more experience and would have continued the injections after the blurring of vision had stopped, more slowly, of course, and with great care. But at that time, the fear of blindness resulting from tryparsamide was a grave consideration.

Among the seven women, three showed marked improvement in all of the symptoms, the disappearance of pains in the joints, a firmer gait, fewer gastric symptoms and a general improvement in general health. Two of the patients had late cases, and one, an early case. One patient showed some improvement over her previous condition. She had an early case of tabes, with severe nerve pains which kept her awake at night. Her pains, though not entirely gone, became bearable, and she has been able to work for one year. Three patients with far advanced cases showed no improvement.

The average age of the thirty-four men suffering from tabes dorsalis was 46 years. The average duration of the infection before any treatment was instituted was sixteen years. Four patients did not know how long they had had the infection. One patient began treatment one month after his primary lesion appeared; one patient began forty years after he had a chancre, presenting a fullblown case of tabes, and although he received continuous treatment for five years, he became progressively worse. Tryparsamide did not help him any more than any other drug, but it invigorated him as none of the other drugs had done, and so he felt happier.

The average number of injections of arsphenamine in this group of men was 23. The smallest number of injections was 8, the largest, 66. Eight patients received no arsphenamine. The average number of injections of mercury was 50. Three patients received 170, 160 and 150 injections, respectively. One patient had only 7 injections. Seven patients did not receive injections of mercury. The average number of injections of bismuth was 24. Seven of the patients had had no bismuth, and 1 patient had 93 injections. The average number of injections of tryparsamide was 22. The greatest number of injections given to one patient was 66.

Of the thirty-four men, eleven showed marked improvement, six of whom had late and five early cases of tabes; six showed improvement, all of whom had early cases; sixteen showed no improvement; of these, fourteen had late cases and two early cases. One of our patients died.

Results of the examination of the spinal fluid are given in the accompanying table. In tabes dorsalis as in other types of neurosyphilis, it will be seen that there is no correlation between the clinical and serologic conditions. If both improve, it is satisfactory. However, I feel that in treating patients, interest lies in clinical evidence, and that physicians have the right to base their impressions of the therapeutic value of a drug on the clinical results rather than on the laboratory results.

Examinations of the Spinal Fluid

	Wassermann Reaction		Colloidal Gold Curve		
	Before Tryparsamide	After Tryparsamide	Before Tryparsamide	After Tryparsamide	Condition After Tryparsamide
1	2+	—	001122100	—	Improvement
2	—	—	001122100	—	Marked improvement
3	4+	—	334454300	000111000	No improvement
4	—	—	001123210	000000000	Improvement
5	—	—	000000000	000000000	No improvement
6	—	—	000000000	000000000	Marked improvement
7	3+	3+	234422111	112211000	No improvement
8	2+	—	144555431	000000000	Marked improvement
9	+	—	000112100	000000000	No improvement
10	4+	2+	334421000	111100000	Improvement
11	3+	2+	334454000	000000000	No improvement
12	4+	+	000111000	000000000	No improvement
13	2+	—	000000000	000000000	No improvement
14	3+	—	332211000	000000000	Improvement
15	4+	2+	334454321	112221100	No improvement

Of the forty-one patients with tabes dorsalis, a little over 36 per cent were markedly improved, 17 per cent improved and 47 per cent unimproved. If those markedly improved and improved are added together, an improvement in 53 per cent of the patients given tryparsamide is found. I have no previous reports with which to compare these figures, for until now tryparsamide has been little used in cases of tabes dorsalis. As I mentioned before, it has been mainly used in cases of paresis, and at most there have been from seven to ten cases of tabes dorsalis reported in every series. In these, the results have varied from 26 to 68 per cent, the latter figure reported by Keith and Le Marquand.[42] Perhaps with an increase in the number of cases of tabes, there will be a corresponding rise in the percentage of improvement, such as occurred in the reports of other types of neurosyphilis.

The combined percentages for the entire series show: marked improvement in 49.8 per cent of the patients; improvement in 28 per cent, and no improvement in 22.6 per cent.

CONCLUSIONS

After reviewing the clinical results in all of these cases, the conclusion seems warranted that tryparsamide is a great aid in combating neurosyphilis, and should be used much more frequently than heretofore. The complications that seemed so great when the drug was first tried have been found to be relatively unimportant. I do not know whether or not we have been unusually fortunate, but we have had no ocular complications in any of our cases. Patients have been carefully examined by the eye department before each series of treatments and, barring exceptional cases, tryparsamide has been used only after a favorable report has been obtained, namely, the absence of contraction of the optic field or a paling of the optic disk. We have had one patient with a mild dermatitis, which we believed was due to tryparsamide. It subsided in a short while, after a few injections of sodium thiosulphate had been given, and did not recur, although the patient received two series of tryparsamide after his recovery. We had one mild nitroid reaction after an injection. This lasted fifteen minutes, but there was none of the severe reactions which so often occur with other arsenical preparations.

The injections have been given at weekly intervals in series of from eight to ten injections of 3 Gm. each. The preparation, which is an N-phenylglycinamide p-arsonic-sodium salt, comes as a clear crystalline powder, which is readily soluble in water. It contains 25.32 per cent of arsenic in the pentavalent form. If it should infiltrate the tissues, it causes burning similar to that experienced with sulpharsphenamine, but causes no necrosis or other injury to the infiltrated area. In fact, some physicians have administered the drug intramuscularly. We have had no experience with this method of administration. We direct our patients to take a physic the night before administration and to refrain from eating for four hours before and for four hours after the injection. This precaution may account for our small number of systemic reactions.

The very nature of this drug and its few ill effects make it ideal for an outpatient and office practice, and it should be used much earlier in the course of the disease than heretofore. In point of fact, since it has such a beneficial clinical effect on lesions of the central nervous system, and since all cases of syphilis are potentially neurosyphilitic, it may be advisable to give a number of injections of tryparsamide in conjunction with injections of arsphenamine, bismuth and mercury, from the onset of the disease, and to continue with it through the whole course of from two to three years of treatment. We have recently begun doing this in our clinic, but only the future can tell whether or not we can reduce by this method the number of patients in whom one of the serious forms of neurosyphilis will eventually develop.

With the patients who come to us with histories of syphilis of long duration and who have tremors, pains in the joints, headaches and increased reflexes, we are beginning treatment almost immediately with tryparsamide, and are obtaining much earlier improvement than heretofore. We are careful to give mercury and bismuth at the same time, or during the period of rest, so as to destroy the spirochete still present. Before giving arsphenamine to an untreated patient suffering from irritation of the nerve, it is much better to give a few courses of tryparsamide, to allay his symptoms.

The concluding sentences of Stokes' article entitled, "The Practitioner and the Treatment of Neurosyphilis," [36] cannot be repeated too often for the welfare of the neurosyphilitic person:

> He [the practitioner] will think tryparsamidly about the resistant case and the preparetic, and will not waste time and tolerance on courses of neo-arsphenamin when the grave trend of a neurosyphilitic involvement once becomes apparent.
>
> He will be appreciative of but not stampeded by malarial and other forms of fever therapy.

I believe that there should not be a modern syphilitic clinic in this country that does not have a large number of its patients under treatment with tryparsamide. The practitioner cannot be urged too often to use it early, frequently and courageously. It can and may be easily forgotten, because it has no dramatic moments like those attained with malarial therapy to fascinate the physician and the public. I also believe that a knowledge of treatment with tryparsamide should be more widely spread in this country, as well as in Europe, by having as many analyzed reports as possible published for comparison.

SUMMARY

1. Tryparsamide is still used relatively little in the treatment of neurosyphilis.

2. This is a follow-up report of the therapeutic result of tryparsamide in seventy-six cases of neurosyphilis. These patients have had no treatment for from one to three years.

3. The group as a whole showed marked improvement in 49.8 per cent; improvement in 28 per cent, and no improvement in 22 per cent of cases.

4. Tryparsamide should be tried early in the treatment of neurosyphilis, especially in ambulatory cases.

5. Ocular changes should be looked for after the use of tryparsamide, as after the use of any other arsenical preparation, but no greater stress should be laid on the possibility of this complication than is customary in the other arsenical preparations. Moreover, a distinction

should be made between subjective and objective ocular changes before discontinuing tryparsamide.

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HAIRLESS MAMMALS

COMPARATIVE HISTOLOGIC STUDIES: PRELIMINARY REPORT *

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In this study five types of genetic hairlessness have been examined histologically: a dominant hairless mutation in the house mouse,[1] and a recessive mutation in the house mouse,[2] the deer mouse,[3] the rat [4] and the rabbit.[5] In addition, a case of hairlessness, apparently inherited although of undetermined genetic nature, has been examined in a house mouse [3] from Cold Spring Harbor, N. Y. The object was to determine the histologic changes occurring in the skin, to trace and compare the development of these abnormalities and to determine if there was any relation between the histology and the type of inheritance.

Of the reports in the literature on hairlessness, that of a hairless goat given by Bonnet [6] and the cases in human beings described by Unna [7] are of especial interest in the present study. The former is similar to the histologic condition found in the dominant hairless type, and the latter, to that found in the other types studied, except that in the rabbit.

MATERIALS AND METHODS

Living animals were observed regularly. Notes were taken and sketches made. Skins were fixed in formaldehyde or Allen's B-15 solution,[7a] and stained with Hansen's or Heidenhain's hematoxylin, respectively. Eosin was generally used for

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counterstaining. Clearing in xylene and embedding in paraffin were found satisfactory. Serial sections, mostly of 10 microns, were obtained. Unstained sections were used for a study of keratinization with polarized light. Whole amounts of pieces of skin, usually unstained, were useful. A few entire skins were examined. Bielschowsky's silver method with pyridine was used for a study of the follicle nerves. The distribution of calcium and potassium was determined by the methods described by Rohdenburg and Geiger.[8]

DESCRIPTIONS

Many of the following details of external description are to be found in the literature cited.

Early Stages.—House mice that are heterozygous for dominant or homozygous for recessive hairlessness and deer mice and rats homozygous for recessive hairlessness acquire the first pelage. At about the time the first hairs have completed formation, shedding commences. In the house mouse this is from about 1½ to 2 weeks of age, in the deer mouse from about 2 to 3 weeks or older and in the rat at about 3 weeks. The house mouse with recessive hairlessness shows the least variation, the deer mouse the most; much variation in the assumption of the pelage and in artificially induced regeneration in the normal deer mouse has previously been reported by Collins.[9] Depilation begins on the head and passes slowly back over the body. Shedding requires about a week or ten days in both types of the house mouse, from ten days to several months in the deer mouse and about ten days in the rat. Mice heterozygous for dominant hairlessness retain the vibrissae and the hair covering the nose, ears, feet, tail and genital region. These hairs are lost in the other types, except in the deer mouse, which keeps its vibrissae and superciliary bristles. Although the other forms mentioned are entirely normal in appearance until shedding has begun, mice heterozygous for dominant hairlessness can usually be detected before this time because of their rough, dull coat. Depilation in the recessive types results from an actual falling out of the entire hair, leaving the body pink and smooth. In the dominant type, however, the hairs break off, usually leaving splintered ends. These stublike, pigmented remains give the animals a characteristic smutty appearance. The skin also generally shows large wrinkles, which are associated with the intensity of pigmentation. Both of these conditions become less apparent in a few days. Pigmented mice homozygous for dominant

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hairlessness show a pigmentation and wrinkling of the skin suggestive of that found in their heterozygous litter mates. In no case, however, do they acquire a real cover of hair. At best they may show a few fuzzy hairs. The feet and tail, on the other hand, show fairly well developed hairs, which are lost at about the time their heterozygous litter mates shed the body hair. Mice homozygous for dominant hairlessness, in contradistinction to the others described, can be identified at birth because of their lack of vibrissae. All of the forms raised extensively in the laboratory (deer mice and both types of house mice) have shown normal weights at birth. Usually by the third or fourth day the weight of mice homozygous for dominant hairlessness falls below normal. Differences in size are readily apparent, and these animals generally become so weakened and emaciated that they die in a few days. The few animals which do mature never attain a normal size. The eyes are apparently defective.

Although mice heterozygous for recessive hairlessness appear normal in all respects, if such animals are also heterozygous for dominant hairlessness, the presence of the factor for recessive hairlessness is expressed in an accentuation of the dominant hairless characteristics. Mice heterozygous for dominant hairlessness and homozygous for recessive hairlessness show first the dominant peculiarities to an exaggerated degree: extreme wrinkling, a rough dull coat, intense pigmentation following shedding and small size. The changes occurring after the loss of hair are largely those characteristic of the recessive type.

Later Stages.—Mice heterozygous and homozygous for dominant hairlessness undergo regeneration of the hair at approximately monthly intervals, as is normal, but the hairs always break off. In the former, most of the hairs remain until the growth of the hair is complete, and a temporary coat is thus formed. As the animals grow older, there is a tendency for the hairs to be formed on only a part of the body at a time. In homogygous mice, the hair breaks off bit by bit as they reach the surface, so that at no time is a dense pelage present. Both forms grow progressively lighter with age, and the skin becomes smooth. The claws of the homozygous mice show dystrophy, but are not elongated. Mice homozygous for recessive hairlessness, between 4 and 5 weeks of age, generally show a sparse fuzzy growth of hairs, many of which are unpigmented. Most of these fall out within a week or so, but at no time after this period does the body completely lack hair. Later regenerations are usually ill defined, but there is evidence of monthly cycles. The vibrissae and the hairs of the feet, the tail and the ears may partly regenerate. The skin becomes whitened and wrinkled. In some cases the eyes may be practically closed owing to enlarged lids. The claws are elongated or hooked, but the teeth

are normal. The deer mice show the same characteristic changes as those found in the house mice with recessive hairlessness, except that the eyelids are unaffected. However, they show a greater variability in the extent of abnormality. The preserved wild hairless mouse from Cold Spring Harbor showed a whiteness and wrinkling of the skin similar to that in the recessive forms. The preserved rabbit was partly haired, especially on the head and feet. The skin was thin and showed only a slight, very fine wrinkling.

Fertility is normal only in the house mice heterozygous for dominant hairlessness. In general, fertility in the other forms is confined to the males, although occasionally a fertile female deer mouse is found. The size of the body is greatly reduced in mice homozygous for dominant hairlessness, but in the other types the seeming smallness is to a large extent due to the lack of hair. All homozygous forms, both dominant and recessive, show a subnormal vitality and are especially sensitive to chilling.

House mice and deer mice homozygous for recessive hairlessness raised in an incubator at about 88 F. show a higher degree of pigmentation than do mice raised under ordinary room conditions. These mice, thus protected, are also much more active and vigorous. Mice homozygous for dominant hairlessness, however, show no improvement.

HISTOLOGY

Dominant Hairlessness in the House Mouse (Mus musculus).—Mice heterozygous for dominant hairlessness show a normal condition of all the layers of the skin. The skin of homozygous mice is thinner, but this is to be associated with the general reduction in size. This type of hairlessness is due to the imperfect formation of hair. Heterozygous mice show varying proportions of hairs well keratinized except for "weak" places, and hairs lacking in keratinization. Nearly all hairs show a bending in the hair canal. Generally, the force exerted by the growing hair is sufficient to push out the bent end, which usually breaks off, at least at the tip. There is a tendency for fragmentation to occur, especially at the weak places. The general extent of such breaking, together with the stage in development at which it takes place, determines the roughness of the coat and the early or late shedding. The less perfectly formed hairs, which usually show no indication of keratinization, remain within the hair canal as bent or coiled and somewhat amorphous masses. These gradually work their way out of the skin, although, even in mice about 10 months old, such remains, now much reduced, can still be detected in the hair canals. The growth of generations of hair after the first seems to be largely responsible for the removal of these remains.

Later hairs usually erupt, although the structure is as imperfect as that of the first hairs. Distortion occurring in the follicles of unerupted hairs is only temporary and disappears after the hairs erupt. The stratum corneum is not a primary causative agent in the abnormal behavior of the hairs. Whereas to a normal hair it offers a resistance only slight enough to produce a temporary deflection of the tip, to these imperfectly keratinized hairs it offers a greater resistance, the strength of which is measured by the weakness of the hair. There is always an association between the amount of hair remaining within the skin and the extent of wrinkling and smutty appearance externally visible. The nerves of the follicles appear normal. Since this type of hairlessness is caused by imperfect keratinization, it may be called "hypotrichosis hypokeratotica."

Recessive Hairlessness in the House Mouse (Mus musculus), Deer Mouse (Peromyscus maniculatus-gambeli) and Rat (Mus norvegicus), and Hairlessness of Undetermined Genetic Nature in the House Mouse (Mus musculus).—The histologic observations in the mouse from Cold Spring Harbor are sufficiently similar to those of the house mouse, the rat and the deer mouse with recessive hairlessness for one to assume that all of these forms represent a common class of abnormality. Until the formation of hair is complete, the potentially hairless mice and rats are also histologically normal. At this time, however, the normal hair club with its broomlike ending is not formed. Instead, various abnormal terminations are found. One of the most common is a split condition of the base in which the ends approach each other in a manner suggestive of a human thumb and finger slightly directed toward each other. The inner root sheath is also generally present around the base of the abnormally ending hair instead of advancing to its somewhat anterior normal position. Furthermore, with the cessation of growth, the follicle does not shorten to just below the sebaceous glands and the location of the club hair, but, as it decreases somewhat in length, the outer root sheath persists as a long slender structure irregular in direction. The initial loss of hair seems to be due to the failure of the hair club to form. This conclusion is based largely on the fact that in the deer mouse the specimens that show persistent patches of hair remaining for a long time possess normal club endings in these hairs.

The reappearance of a complete cover of hair is prevented by changes in the follicles. With the initiation of growth of the second generation of hair, there is a tendency in a varying number of follicles for the lower part to become separated from the upper part. If this occurs before the differentiation of hair has begun, a cystic formation results. Later separation gives rise to hairs which either end blindly

in the skin or, no longer having the passageway afforded by their own hair canals, force an abnormal exit through the epidermis. The hairs which continue through their own follicles form all possible angles with the surface as they leave the skin. The nonerupting hairs and those which force an exit only after considerable growth in the skin are always surrounded in their unsheathed portions by infiltrations of cells. These appear to consist of polymorphonuclear leukocytes, eosinophils, nuclei from the surrounding tissue and transformed follicle cells. Not all follicles are active during the initial regeneration. A few growing hairs are always to be found in the skin after this time, and these account for the continual presence of the few scattered hairs always visible externally. Irregularity in direction of both follicles and hairs is especially characteristic of animals with this type of hairlessness.

Cysts are formed not only from the ends of the follicles already mentioned, but also frequently in the follicle surrounding the growing portion of a nonerupting hair. The sebaceous glands are hypertrophied and likewise give rise to cysts. The cysts so far mentioned are located in the subcutis after they are mature. The hair canal may also be cystically enlarged, and is always packed with concentrically arranged stratum corneum, which offers a strong contrast in appearance to the very sparse stratum corneum-like material found in the other cysts. The arrangement of the stratum corneum indicates its formation from the walls of the hair canal.

Hairs remaining within the skin undergo disintegration and resorption. The exact nature of this process has not been determined, but after disintegration has taken place, pigment granules can be seen located within cells which appear to have originated from the surrounding tissue and from the outer root sheath of the follicle.

These changes necessarily alter the appearance of the layers of skin. The subcutis is practically filled with infiltrations of cells and with cysts. When the latter are present in the corium, or when the hair canals are cystically enlarged, a compression of the corium tissue is found. The musculi arrectores pilorum are frequently dislocated. The thinness of the subcutis, which is more noticeable in mice showing slight formation of cysts, seems to be largely due to the lack of general growing periods of the follicles. Normal mice during nongrowing periods also have a thin subcutis, which is enlarged during growth by an increase in both the size and the number of fat cells.

The swelling of the eyelids, especially conspicuous in the rats and in most of the house mice with homozygous recessive hairlessness, is caused by an excessive cystic enlargement of the meibomian glands.

In the house mouse and the deer mouse with recessive hairlessness the nerves of the follicles appear normal. The isolated cysts are supplied with nerves. The deposits of calcium and of potassium are also normal, except that both of these elements are found abundantly in the cysts.

Since the continued lack of hair characteristic of these animals appears to result largely from the formation of cysts, this condition may be called "hypotrichosis cystica."

Cross of Dominant by Recessive Hairlessness in the House Mouse.—In general, doubly heterozygous mice show the characteristics of the heterozygous dominant condition. Unlike these, however, and like mice homozygous for recessive hairlessness, some mice may show a pronounced cystic enlargement of the hair canal. Mice which are heterozygous for dominant hairlessness and homozygous for recessive hairlessness show the action of both factors: the imperfect formation of hair, abnormal club hairs and irregularly directed slender follicles, peculiar to the first generation of hair, and unerupting and disintegrating hairs, and cystic formations, found in later stages. However, all of these conditions are intensified, as might be expected from the exaggerated external peculiarities. The large number of coiled and bent hairs remaining within the skin following shedding accounts for the early shedding, extreme wrinkling and intense pigmentation so pronounced in the living specimens. Except for these remains of hairs, which, with an increase in age, are practically eliminated, skins from old animals show a histologic condition similar to that in the most extremely abnormal animals homozygous for recessive hairlessness.

Recessive Hairlessness in the Rabbit (Lepus cuniculus).—The one preserved specimen examined showed a partial agenesis of follicles. The skin and all its layers, except for a thin subcutis, were normal. The follicles were irregularly directed and tended to form circles. All of the hairs erupted and were normally keratinized. The sebaceous glands were normal, but the musculi arrectores pilorum were poorly differentiated or lacking. In places there appeared to be a slight hypertrophy of the stratum corneum. Hairlessness in this instance might be called "hypotrichosis hypoplastica follicularis."

CONCLUSIONS

From a comparison of the reports on the various animals studied, it is evident that the skin responds to different conditions in a limited number of ways. The conditions which induce hairlessness may be noninherited, may sometimes be only temporary or may be inherited. The follicles, especially by undergoing the formation of cysts, and the

epidermis, with its proliferation of stratum corneum, play important rôles in cases of hairlessness following the loss of the lanugo. If the lanugo is deficient or abnormal, there may be a partial agenesis of the follicles or an imperfection of the structure of the hair. In the cases of inherited hairlessness reported here, hairlessness was due to a partial agenesis of the follicles, to the imperfect structure of the hair or to degenerative changes, largely of a cystic nature, following the appearance of the lanugo, which revealed its imperfect nature only on close examination.

Dr. L. C. Dunn furnished the recessive hairless house mice used in this study, and Dr. N. G. Lebedinsky furnished the dominant hairless house mice which I secured indirectly through Dr. W. E. Castle. Dr. H. W. Feldman provided the deer mice and Dr. Elmer Roberts and Mr. L. C. Thomas the preserved and living specimens and photographs of the rats. Dr. A. D. Kislovsky and Dr. Kondireff provided the preserved hairless rabbit, and Dr. Clyde E. Keeler the preserved normal rabbits. Dr. George D. Snell provided some offspring of a cross of the dominant by recessive hairless house mice, and Dr. A. M. Banta of the Carnegie Institution, the preserved hairless house mouse caught in Cold Spring Harbor, as well as the photographic plates. Dr. Walter Landauer, under whose direction this work was done, gave invaluable advice.

THE BLOOD IN PSORIASIS

WITH SPECIAL REFERENCE TO CALCIUM, PHOSPHORUS AND POTASSIUM *

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The etiology of psoriasis has been the impelling motive for much elaborate research and the occasion of many hypotheses. These hypotheses have invoked every conceivable irregularity in the human economy, including the diet, sensitization, both bacterial and fungous infection, neurotrophic, endocrine dyscrasia, anaphylaxis and heredity.

All sorts of appellations have been assigned to this disease. For instance, Schamberg [1] referred to it as the "dermatologic mystery," and while he expressed a belief in familial incidence, he did not favor the theory of heredity. He assigned rheumatism, gout, defective elimination, defective assimilation of food, pancreatic disease, digestive and nutritional disorders, disturbances of the nervous system, fright, shock, neurotic conditions, tuberculosis, endocrine disturbances, parasitism and disorders of metabolism as possible causes of this mystery. Of this group of possible causes, he expressed the belief that the rheumatism is so often associated with the disorder that it must have some relationship, but that gout and disturbances of the endocrine glands can easily be eliminated. With Dr. Kolmer, Dr. Raiziss and Dr. Ringer, he conducted extensive research which seemed to indicate a retention of nitrogen in cases of psoriasis. He also conducted studies regarding the content of the blood in cases of psoriasis, with special reference to phosphorus, calcium, magnesium and potassium, and he found no deviation from normal. He divided the progress of the disease into three stages: (1) progression or evolution, (2) quiescence and (3) spontaneous involution or regression. He is a strong advocate of a diet low in protein, urging that the patient be put on a diet that contains not more than 4 Gm. of protein daily.

A rather unusual, and I feel somewhat exaggerated, view is held by Lévy-Franckel and Juster,[2] in which they suggested that the hereditary and familial transmission of psoriasis is due to syphilis, which may

* Submitted for publication, Jan. 23, 1931.

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1. Schamberg, J. F.: Survey: The Known and Unknown About Psoriasis, J. A. M. A. **83**:1211 (Oct. 18) 1924.

2. Lévy-Franckel, A., and Juster, E.: Hereditary and Familial Psoriasis, Médicine **7**:128 (Nov.) 1925.

create a special cutaneous, glandular or humoral predisposition, such as syphilitic dystrophia. They held that the action of syphilis in this type of case is dystrophic and not microbian, as is seemingly proved by the fact that cases of conjugal psoriasis are almost unknown.

Both Kreibich [3] and Ström [4] favored the idea of neutrotrophic disturbances; the former reported a case of severe psoriasis of long standing that disappeared on one side after a gunshot wound of the shoulder. The latter author reported a case from the Roentgen Institute of Stockholm accompanied with clinical notes and roentgenograms of associated destructive and atrophic changes of the bones of the fingers and toes. The patient was a man, aged 50, who showed typical psoriasis of twenty years' duration, with the nails greatly thickened and fluted and with arthritic deformities and disabilities of the affected fingers and toes, which were swollen and showed a loss of active mobility. There were rarefaction and destruction of the distal and proximal portions of the terminal phalanges and destruction of the articulating cartilages. Ström notices a similarity in the skeletal changes of this condition to those found in vasomotor trophic neuroses, such as scleroderma and Raynaud's disease, and certain nervous disorders, such as syringomyelia and lepra nervosum.

The endocrine theory has as its supporters, among others, Aja and Portilla,[5] who nine years ago reported a case from Madrid in which there was complete involution of the psoriatic lesions after the use of ovarian extract. Radaeli [6] said that while he believes in the relationship between the glands of internal secretion and psoriasis, and that there is some dependence on the vegetative nervous system, he has not been able to note any consistent results obtained from irradiation of the thymus by the method of Brock or the exposure of the lumbar and lower dorsal parts of the spine.

The belief in the infectious etiology of psoriasis is constantly under discussion, including all the logical infective possibilities; whether the considerations are cursory or exhaustive, one finds pathologic as well as saprophytic organisms associated with the lesions, but to isolate any one of these and successfully incriminate it with the sole responsibility for the disease needs at least further consideration. After considerable work in an endeavor to isolate *Spirochaeta sporogona,* Oelze [7] reported

3. Kreibich, C.: The Pathogenesis of Psoriasis, Arch. f. Dermat. u. Syph. **124**:665, 1918.

4. Ström, S.: A Case of Psoriatic Arthropathy, Acta radiol. **1**:21 (July) 1921.

5. Aja and Portilla: Psoriasis and Hypogenitalism, Soc. Dermat. & Syph., Madrid, Oct. 14, 1921.

6. Radaeli, A.: Assumed Etiologic Relations Between Endocrine Changes and Psoriasis, Gior. ital. di dermat. e sifil. **67**:1130 (Aug.) 1926.

7. Oelze, W.: A Note on Spirochaeta Sporogona Psoriasis Rasck—the Alleged Cause of Psoriasis, Berl. klin. Wchnschr. **58**:578, 1921.

that all of his tests gave negative results, and that the accused organism eluded every method of staining that he was able to find. Prantor [8] concluded that since several of his patients recovered as a result of the use of emetine hydrochloride, some protozoan must be accused as the cause of this disease. Marcus,[9] by removing the scales of the psoriatic lesions and sterilizing them by washing in from 70 to 90 per cent alcohol and then introducing them into a culture medium kept at 37 C., produced cultures and *Sarcina* in 95 per cent of the cases. Only 5 per cent of the tests proved to be negative; 12.5 per cent also showed staphylococci; 7.5 per cent, diplococci; 5 per cent, *B. subtilis,* and 5 per cent, *B. pseudodiphtheria.* Bory [10] also expressed a belief in the infectious origin of psoriasis. He concluded that insects may be the carriers of the still unknown germ of psoriasis, and since he had found that specimens from lesions of psoriasis stained with polychrome methylene blue have constantly shown small, irregular, rodlike germs resembling mycelia, and in appearance much like the threads of *Microsporon minutissimum,* he felt that this may be the offending factor. Saunders [11] succeeded in isolating *Monilia* from the skin, scales, mouth and sputum in psoriasis. Interesting as the conclusions and beliefs of these observers may be, it remained for Morgenstern [12] to advance the idea that psoriasis is but one of the manifestations of a generalized condition of the body and that the arthropathies that occur with it would correspond to a secondary or tertiary stage. Samberger [13] spoke of a parakeratotic diathesis that gives rise to psoriatic lesions, whereas in the skin of a normal person pyodermia might have ensued, and he said that the employment of the thymus extract and the Brock fractional exposures to the roentgen rays merely stimulated the general skin, making it more resistant to the irregular formation of cells.

A few cases have been reported in which the systemic involvement might be questioned, as there appeared only one or two small, continuously localized lesions that might make one consider the traumatic or infectious origin of the disease. Hoffmann [14] spoke of the case of a

8. Prantor, V.: Psoriasis: Case Report, Wien. klin. Wchnschr. **34**:303, 1921.

9. Marcus, M. A.: Sarcinae in Psoriasis, J. Lab. & Clin. Med. **11**:967 (July) 1926.

10. Bory, Louis: On Parasitic Theory of Psoriasis, Bull. Soc. franç. de dermat. et syph. **7**:278, 1919.

11. Saunders, G. G.: Case of Psoriasis; Isolation of Monilia from Skin, Scales, Mouth and Sputum, Lancet **2**:1226 (Dec. 12) 1925.

12. Morgenstern, J.: Arthropathica, Psoriatic Arthritis and Psoriasis in Diseases of Joints, Wien. Arch. f. inn. Med. **12**:273 (Feb.) 1926.

13. Samberger, F.: Concerning the Nature of Psoriasis, Acta dermat.-venereol. **2**:359 (Nov.) 1921.

14. Hoffmann: Chronic Familial Psoriasis Limited to Small Area of the Skin, Arch. f. Dermat. u. Syph. **135**:228, 1921.

woman in whom the psoriasis was limited to the toe for several years; a limited eruption later developed on the fingers and scalp of the son. The author suggested the possibility of a dermatrophic virus, which he thought might also be arthrotrophic. Sowade [15] referred to the case of a man, aged 30, in whom a small isolated patch of psoriasis developed on the genitalia. Repeated Wassermann tests, as well as negative clinical evidence, ruled out syphilis.

Thus, one may consider that the problem resolves itself to a study of the constituents of the blood with special reference to calcium, potassium and phosphorus, and the effect on those elements resulting from the use of parathyroid extract enterally and parenterally.

The use of parathyroid extract is usually dated from the work of Collip in 1925, but Berman [16] reported similar researches in the proceedings of the Society for Experimental Medicine and Biology in 1924. In this report, unless otherwise indicated, the material used was the parathyroid extract (Collip).[17]

The pathology of psoriasis is too well recorded in the literature [18] and various texts to require extended consideration here. The burden of my discussion rests on the possible etiologic factor as found in the blood and the mechanism of this factor in the production of the well known pearly scales of psoriasis.

The question of the site of the agent that provokes the lesions of psoriasis may be considered either from the standpoint of the content of the blood, which would make the walls of the vessels sufficiently permeable to allow the diapedetic egress of the cells, or according to the view of a change in the walls of the vessels which might be due to some alteration in the nervous regulation of this wall and by which the exocytosis could be accomplished. I decided to take the first part of this problem, or that of the composition of the blood, for the first attack and follow up later with other lines as they might present themselves.

Specimens of the blood of 126 patients have been studied. The patients were from all walks of life and all strata of society, from the poorest persons who could not supply the needed demands in diet to those who were able to have anything in the way of medication, rest, diet or change of scene and climate to help accomplish the end.

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15. Sowade: Isolated Psoriasis Eruption, Tr. Vienna Dermat. Soc., Feb. 9, 1922.

16. Berman, L.: Separation of Internal Secretion of Parathyroid Glands, J. Lab. & Clin. Med. **11**:412 (Feb.) 1926.

17. The particular preparation used in this series of experiments was the parathormone (Lilly).

18. Civatte, A.: Psoriasis and Seborrheic Eczema, Pathological Anatomy and Diagnostic Histology of Two Dermatoses, Brit. J. Dermat. **36**:461 (Nov.) 1924.

METHOD

Each patient was examined at the time of the first call, and a complete history was taken as to former illnesses and the duration of the present disease. A family history was made, and items that might have bearing on the case were carefully recorded and tabulated.

The next step was the taking of specimens of blood for analysis. At first this was done in the usual way, with drawing 30 cc. of blood into a sterile syringe and then transferring this in the usual manner to a large test tube. This technic allowed a sufficient change in the inorganic elements in the blood plasma to produce appreciable error. This difference in the constituents was due to the change in the environment of the red blood cell, as it was transferred from the blood vessel to the tube. The decrease in the carbon dioxide of the normal air as compared with the carbon dioxide of the blood caused a change in the concentration of the potassium of the plasma as it sought equilibrium between red cell and plasma, thus increasing the potassium in the plasma and producing the abnormally high reading for potassium. After this source of error was discovered and the cause was recognized, the samples of blood were withdrawn in a dry syringe that had been cooled to room temperature and then discharged through a very small rubber tube into a glass centrifuge container in which 3 cc. of liquid petrolatum had been placed, the rubber tube being immersed under this oil as the blood was discharged from the syringe. This container was allowed to stand for about one hour and was then centrifugated at 1,500 revolutions per minute for fifteen minutes. In this way the blood was drawn, centrifugated and collected as clear serum free from blood cells before it came in contact with the air. It was found that if the syringe were wet, there was a much greater possibility of hemolysis, which made the determinations of potassium less accurate, and it was more difficult to identify the end-point reaction.

With the blood serum now collected clear and free from all cells, it was divided into six portions for analysis. In the determinations of calcium the method of Clark and Collip [19] was used, which is a modification of the Kramer-Tisdall method and consists of precipitating the calcium direct from the serum as oxalate which is later titrated with potassium permanganate. A blank was run with each series of precipitations and titrations to determine the factor of error. With few exceptions, each specimen of blood was run in duplicate as a check for possible technical error.

The phosphorus was determined by the method of Fiske and Subbarow [20] on the principle that the phosphates react with ammonium molybdate to form ammonium phosphomolybdate. This ammonium phosphomolybdate is reduced by aminonaphthosulphonic acid to a blue compound that is estimated colorimetrically.

The potassium, which was by far the least satisfactory of the three from the point of accuracy, was determined by the method of Kramer and Tisdall.[21] In this method the potassium is precipitated as cobaltinitrite, and the latter is titrated with potassium permanganate.

The specimen of every patient's blood was analyzed at least once when the patient was first seen, or at the beginning of the treatment selected for that

19. Clark, E. P., and Collip, J. B.: Modification of Kramer-Tisdall Method, J. Biol. Chem. **63**:481, 1925.

20. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.

21. Kramer, B., and Tisdall, F. F.: Determination of Potassium in Serum, J. Biol. Chem. **46**:339, 1921.

particular case, before medication was administered. Most of the blood was analyzed twice and some as many as five times.

RESULTS

In the first series of analyses the calcium and the phosphorus ran in harmony with each other; as the one rose so did the other, and as the one showed a lowering, there was a depression in the other. Considering the normal amount of calcium as between 9 and 11 mg. per hundred cubic centimeters of blood serum, as determined by Clark and Collip [19] and others, it was found that in 126 cases the determinations of calcium resulted as follows: normal calcium, 67 cases (53.17 per cent); hypercalcemia, 36 cases (28.57 per cent); hypocalcemia, 23 cases (18.26 per cent).

From these figures it must be deduced that the variation in calcium, at least of the diffusible type, shows no marked alteration from that in normal persons apparently in good health.

The work with potassium, while not entirely satisfactory from the standpoint of accuracy of determinations, agreed with the work done some years ago by Yanagi [22] in which he found that the potassium in the blood plasma, in its quantitative determinations, was antagonistic to the calcium, making its deviations in opposite directions to calcium irregularities. After analyzing more than fifty specimens of blood for potassium and finding no change that gave any light on the problem and in view of the unsatisfactory manner of making these analyses, this part of the problem was abandoned.

In order to determine the possibility of altering the inorganic constituents of the plasma by various forms of manipulation, the series of cases was divided into ten groups, including 105 cases: 97 cases of psoriasis, and 8 cases in which the persons were free from the disease. Twenty-one patients with psoriasis had been so irregular in their attendance or had been seen but once when the first specimen of blood was taken that they were not considered as relevant to the problem. The ten groups will be considered in order.

The first group was composed of 8 healthy males who were tested by analyses of the blood made at two different times under similar circumstances to check up a possibility of normal variations. The results of these analyses are shown in table 1.

A variation is seen in the values obtained for calcium, from 9.4 as the lowest to 11.4 as the highest, but the majority of values lay between 9 and 11. It will be noted from table 1 that the general rule applies

22. Yanagi, K.: Antagonism Between Potassium and Calcium Ions Observed from Their Effect on Gas Metabolism of Blood, Tohoku J. Exper. Med. **5**:111 (Aug.) 1924.

that as the calcium is lowered the phosphorus descends with it, while the potassium begins its ascent, or the same relation in opposites may be the case.

In the second series, consisting of 12 patients with psoriasis whose second analysis of the blood was made after a series of from four to six exposures to the ultraviolet light under the air-cooled lamp, given at intervals of three days for a sufficient length of time to produce a mild but positive erythema about five hours after exposure, the blood plasma showed an average increase of 1.2 mg. of calcium per hundred cubic centimeters of plasma. All of these patients showed at least temporary improvement in symptoms.

The third group consisted of 15 patients with psoriasis to whom, for a period of one month, parathyroid extract in combination with calcium lactate was administered. The tablets, containing 1/20 grain

TABLE 1.—*Analyses of Specimens of the Blood from Healthy Males to Determine Normal Variations*

Identification	Calcium		Phosphorus		Potassium	
	1	2	1	2	1	2
A	9.4	10.1	3.1	3.2	17.0	16.4
B	10.5	10.3	3.5	3.5	16.0	19.4
C	11.0	10.5	3.7	3.6	22.0	18.0
D	11.2	11.3	3.6	3.8	17.0	17.0
E	11.0	11.4	3.4	3.1	15.0	17.0
F	*	9.9	3.1	2.46	16.4	20.9
G	10.6	10.8	3.1	3.5	23.7	19.0
H	10.2	*	3.3	2.13	19.8	18.9

* Errors in reading made abnormally high values, so they are not recorded; 0.5 mg. was allowed for technical variation or error in the readings.

(0.00324 Gm.) of parathyroid extract and 2 grains (0.13 Gm.) of calcium lactate, were given by mouth twice a day, morning and evening. The patients showed irregular results; some showed a decrease and others a gain in the calcium coefficient. There seemed to be no regularity to the loss or gain. The maximum gain was 1.1, while the maximum loss was 1.8. In these cases other factors probably produced more effect than did the small doses of the parathyroid extract passing through the intestinal tract.

The fourth group consisted of 4 patients with psoriasis who were given ephedrine hydrochloride and calcium lactate by mouth. The ephedrine was administered as a result of the supposed relationship between the thyroid and parathyroid and the suprarenal glands and the effect they have on the sympathetic nervous system. The dosage was 3/8 grain (0.0243 Gm.) of ephedrine hydrochloride with 5 grains (0.324 Gm.) of calcium lactate given three times a day for three weeks. There was no determinable change in the constituents of the blood in any of these patients, and no visible clinical improvement was noted.

In the fifth class are included the cases of 10 patients with psoriasis, most of which had been extremely stubborn in response to therapy. They were cases of long standing with few or no remissions in the last eight or ten years, even during the summer. To this class subdermal injections of parathyroid (Collip) were given twice a week, the first injection being 0.5 cc., and each succeeding injection being 1 cc. At the same time, 10 cc. of calcium gluconate was injected intramuscularly into the gluteal muscles, each injection being alternated right and left. Without local applications and without other concurrent methods of treatment, this group of patients showed the most consistent rise in calcium of any of the groups and also the most consistent clinical improvement of any of the groups. Table 2 shows these changes in the content of the blood.

TABLE 2.—*Calcium Content of the Blood in a Group of Patients with Long-Standing and Refractory Cases of Psoriasis Treated Only by Subdermal and Intramuscular Injections*

	Calcium			
Identification*	1	2	3	4
A	10.80	13.80	10.5	
B	10.40	12.30	11.1	11.4
C	8.01	12.40	10.8	
D	9.01	11.30		
E	9.90	10.20		
F	10.00	10.50		
G	9.68	10.20		
H	7.90	9.29		
I	10.60	10.50		
J	9.20	10.20		

* Patients A and C, after showing marked improvement, at the time of the second analysis encountered difficulties that gave rise to nervous and digestive disorders with corresponding changes in the blood and clinical manifestations.

In the sixth group were 9 patients who were given calcium gluconate in the same dosage and frequency as those in the fifth class but without the parathyroid extract. There was no appreciable increase in the calcium content of the blood, though there was improvement in the patients clinically. So far as results could be obtained in this group, they simulated closely those of the third group in which the changes in the blood are irregular and not according to any consistent findings of a rise or a depression.

In the seventh group there were 20 patients who were treated with external applications only. Among these applications were included ammoniated mercury ointment, 5 per cent chrysarobin in traumaticin, saturated solution of chrysarobin in chloroform, ointment of crude coal tar and ointment of sulphur. There was no discernible change in the content of the blood in this group, with the exception of 2 patients who suffered from a severe dermatitis from the chrysarobin paint. In these 2 patients the blood was taken at the height of the dermatitis and

was found to be high in both calcium and phosphorus, having risen in one case from a calcium factor of 9.3 to one of 10.5, and in the other from 8.7 to 9.9 during the dermatitis.

Group 8 is made up of 16 patients whose major treatments consisted of the Brock irradiation of the thymus, thyroid and parathyroid glands. In every one of these cases there was recorded a slight increase in the amount of calcium in the blood plasma, though in one it amounted to only a small amount (0.1 mg.), which might easily have been within technical error. There was also a clinical improvement in every case.

In group 9 there were 3 patients for whom determinations of calcium were made every two weeks for five analyses. The values for calcium and phosphorus are best given in tabular form (table 3).

During the period of the first three analyses, patient A showed marked improvement; then a slight recurrence occurred and remained on this level until the time of writing, in spite of the calcium being

TABLE 3.—*Group of Patients on Whom Determinations of Calcium Were Made Every Two Weeks*

	Analyses									
	1		2		3		4		5	
Identification	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus
A	8.6	3.6	10.2	3.3	13.8	2.1	10.4	3.2	10.6	3.5
B	9.8	3.1	12.2	2.6	10.6	3.6	10.1	3.09	10.4	3.2
C	10.4	3.4	12.3	2.6	11.1	2.6	11.4	3.1	11.5	3.7

within normal range. Patient B showed a rapid increase of calcium in the first two weeks, with marked improvement in the clinical signs. She was free from the eruption, with the exception of a few dull red spots that were becoming less pronounced every day. After the second week, the acute rise in calcium from 9.6 to 12.2 began to subside, and the values fell to a little above 10.1 and remained there, with continued clinical improvement. The values for patient C followed closely those for patient B.

The last group consists of 6 patients who were given a course of parathyroid extract (Collip) for two and a half weeks, with intramuscular injections of calcium gluconate; the patient was then subjected to air-cooled ultraviolet light sufficient to cause erythema. At the time of writing, only two determinations had been made on these patients, and whether the increase in calcium was due, as in group 5, to the parathyroid plus the calcium gluconate alone or whether this action was enhanced by the ultraviolet light cannot be told at this time, but clinically these patients have shown more rapid improvement than those in group 5.

To eliminate, then, the groups in which indecisive results have been obtained, one could without loss of value subduct group 3, the patients receiving parathyroid by mouth; group 4, those receiving ephedrine and calcium lactate by mouth; group 6, those receiving only intramuscular injections of calcium gluconate; group 7, those receiving only the administration of local applications, and groups 1 and 9, which were merely control groups. This leaves groups 2, 5, 8 and 10. Combining groups 2, 5 and 10, or those using the ultraviolet light alone, those using parathyroid and calcium gluconate together and those using parathyroid extract, calcium gluconate and ultraviolet light, and considering in addition to this group 8, in which the thymus, thyroid and parathyroid glands were stimulated by the x-ray according to the method of Brock, the agencies at work have been reduced to the endocrines and the calcium balance as carried in a usable form in the blood plasma. As the diffusible calcium is seen to vary as much in the blood of the normal or apparently healthy persons as it does in the blood of those affected with psoriasis, and, furthermore, as there is a rise in the diffusible calcium, at least for a time, in the patients who show clinical improvement, one is led to assume that there is a possible relationship in the symptoms of psoriasis and the calcium content of the blood plasma. This calcium may be in diffusible, nondiffusible or combined form. Table 3, which gives the results of analyses of specimens of blood, was subjected to five analyses over a period of ten weeks, shows a marked temporary rise for the first two weeks and then a reduction to normal. There is evidence of a disturbance of some mechanism, such as a possible specific combined protein molecule, which, disturbed by the various methods of treatment, such as parathyroid and calcium, the ultraviolet light or the Brock method of irradiation, breaks down in part to give temporarily a larger calcium content in the plasma, but as soon as this mechanism establishes its equilibrium, it continues to supply the needed calcium, as is shown by the clinical improvement, but only to the point at which the calcium balance of the normal plasma is again restored.

According to Kirk and King,[23] the inorganic constituents of the blood may be present in three forms: ions, dissociated molecules in equilibrium with the ions and nonionizable compounds with some organic constituents. It has also been shown by these investigators that all of the common inorganic constituents of pigs' serum are totally diffusible, with the exception of calcium. The nondiffusible part of the calcium of the blood has long been recognized as being from 25 to 50 per cent. Hastings, McIntosh and Salvesen [24] found that it is as hard to increase

23. Kirk, P. L., and King, C. G.: Calcium Distribution in Blood, J. Lab. & Clin. Med. **11**:928 (July) 1926.

24. Hastings, A. B.; McIntosh, J. F., and Salvesen, H. A.: Effect of Administration of Calcium Salts on Inorganic Composition of Blood, J. Biol. Chem. **60**:327 (June) 1924 (charts).

the blood calcium in patients with blood low in protein as it is to increase normal blood calcium, apparently because the concentration of protein is the dominating factor which determines the upper limit for the amount of calcium the blood is able to dissolve. This is not in complete harmony with the findings of Cameron and Moorhouse,[25] who expressed the belief that the difference of calcium content in the blood plasma is largely due to the lowering of the threshold for the excretion of calcium in the intestine. In conditions such as nephritis with uremia, diminished plasma protein was accompanied with a marked fall in the calcium content, though tetany did not result, while following parathyroidectomy the decrease in serum calcium was not accompanied by diminution of serum protein. Hence, they concluded that the lowering of serum calcium in parathyroid tetany is chiefly due to a change in the "ionized calcium." This may account for discrepancies in the calcium balance in psoriasis as it does in rickets, in which, in spite of the normal calcium constituents of the plasma, it is known that there is a disturbance in calcium which therefore must be in some form of the combined calcium or plasma protein. Cameron and Moorhouse found that the calcium in the cerebrospinal fluid is between 6 and 7 mg. per hundred cubic centimeters, which is in rough agreement with the proportion of plasma calcium considered diffusible. In tetany, the amount of calcium in the spinal fluid is low. The average true diffusible calcium in the blood plasma of normal dogs is 53 per cent of the value for serum calcium. After parathyroidectomy the calcium of the whole blood definitely decreases; the decrease effects both the diffusible and the nondiffusible calcium. The constancy of calcium in the blood is due to a reservoir of calcium salts in bone, and a kidney and intestinal "dam" of excretion. In calcium starvation the reservoir of calcium in the bone is drawn on. Cameron and Moorhouse expressed the belief that in normal blood plasma there is an organic calcium compound which, when all of the calcium ions are removed, slowly dissociates. Such a compound is usually assumed to be a protein combination, but the organic radical must be specific and not one of the ordinary plasma proteins. They termed the calcium protein X and gave the formula of $CaX = X^{--} + Ca^{xx}$ or an equilibrium of dissociation. They also constructed the following formula:

$$\frac{(X^{--}) \times (Ca^{xx})}{CaX} = k \text{ (a small constant)}$$

If, under normal conditions, the amount of X is constant, then since normally excess calcium reaches the blood stream from the diet, one can perhaps consider that the maximum amount of CaX will be formed,

25. Cameron, A. T., and Moorhause, V. H. K.: Calcium, J. Biol. Chem. **63**: 687, 1925.

and this will hold a definite concentration of calcium ions in equilibrium in the plasma. Other interlocked equilibria will be set up with bicarbonate, phosphate ions, etc., resulting in the formation of definite amounts of unionized inorganic calcium compounds. In the presence of an excess of calcium ions, the series of equilibria will ultimately depend on the organic compound X, which can unite with calcium, and excess calcium will be excreted or flow away. The constancy of the blood calcium depends on an adequate supply of calcium from the diet, and on the presence in the blood of a specific organic compound (X), which unites with calcium and dissociates only slightly. They expressed the belief that Collip's parathyroid hormone probably controls the formation of the organic compound X.

After much research with normal animals, Greenwald and Gross [26] held that it is highly probable that the parathyroid hormone liberates calcium from some noncaseous tissue and that some attending mechanism draws on the calcium of the bone to supply the deficiency thus created.

Under normal conditions and in the human subject the question arises as to how this hypersecretion of parathyroid may be affected. It has been assumed that the x-ray does have a stimulating effect on glandular tissue if it is given in very small doses, but that it has a paralyzing effect when given in large doses. Grant and Gates [27] showed that irradiation of the parathyroid of rabbits caused hypertrophy of the gland, and that when there was a partial parathyroidectomy of the hyperplastic tissue, the remaining portion was potentially active, resulting in an increased factor of safety, showing less loss of calcium and an absence of rise in the inorganic phosphorus of the blood serum, usually seen in complete parathyroidectomies.

If, then, the parathyroid may be stimulated by small doses of the x-ray with the effect of producing an increase in the output of the parathyroid hormone, there is this means of supplying this factor of the necessary group of factors to assist in the production of the plasma protein X, which hypothetically may be considered as absent or decreased in psoriatic patients. Not infrequently the psoriatic patient is markedly improved during an attack of some acute illness, such as an infection accompanied by fever. Bircher and McFarland [28] of the Mayo Founda-

26. Greenwald, I., and Gross, J.: Effect of Long Continued Administration of Parathyroid Extract Upon Excretion of Phosphorus and Calcium, J. Biol. Chem. **68**:325 (May) 1926.

27. Grant, J. H. B., and Gates, F. L.: Effect of Ultraviolet Light Upon Content of Calcium and Phosphorus in Parathyroidectomy, J. Exper. Med. **45**:115, 1927.

28. Bircher, Max, and McFarland, A. R.: The Globulin Content of the Blood Serum in Syphilis, Arch. Dermat. & Syph. **5**:215 (Feb.) 1922.

tion found that with every acute infection there was an increase in serum globulin. With this increase in globulin there would also be an increase in what has previously been termed the specific plasma protein X, and this would account for the frequent improvement during fevers. The reason for exacerbations in the psoriasis with arthropathies may be due to the lowering of the calcium threshold in the kidney and intestine, for in cases of arthritis there is always an increase in the excretion of calcium and urea.

Many discussions have arisen as to the possibility of feeding calcium with the intent of raising the inorganic calcium in the blood serum. In a large number of the contributions, the negative contention is held. In the work of the past three years, it has been proved in numerous instances that the calcium could be increased by proper diet and by direct administration of various preparations of calcium, especially the calcium gluconate. These observations are not in accord with those of Denis and Corley,[29] who found no elevation of the serum calcium in rabbits fed doses of calcium chloride and calcium lactate daily and no higher calcium content in the tissues than that in control animals. Halverson, Mohler, Bergun and Clark[30] showed that no increase occurred in the calcium content of blood in animals given a rich calcium diet or calcium with their food. Denis and Minot[31] reported that the blood calcium of normal human subjects was not elevated by the ingestion of 6 Gm. of calcium lactate daily for a period of ten days. The probable reason why these investigators did not note a rise in calcium was that they failed to make sufficiently frequent analyses of the blood. Kahn and Roe,[32] however, supported my observations when they stated that if calcium is given orally in quantities of 20 Gm. in 300 cc. of water and the estimation is made every hour for seven hours, an elevation between 60 and 75 per cent will occur between the third and fifth hour after ingestion, with an average maximum elevation of 81 per cent between the fourth and fifth hour, and that the content returns to normal by the tenth hour. Making many experiments, they found that 5 Gm. was the optimal dose, and that the return to normal occurred between the eighth and fourteenth hour after ingestion, so that to obtain the greatest possible efficiency, calcium given by mouth should be given in doses of 5 Gm. every four or five hours during the day.

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29. Denis, W., and Corley, R. C.: J. Biol. Chem. **66**:609 (Dec.) 1925.

30. Halverson; Mohler, Bergun, and Clark: J. Biol. Chem. **32**:171 (Nov.) 1917.

31. Denis, W., and Minot, A. S.: J. Biol. Chem. **43**:89 (Aug.) 1920.

32 Kahn, B. S., and Roe, J. H.: Calcium Absorption from Intestinal Tract in Human Subjects: Experimental Study, J. A. M. A. **86**:1761 (June 5) 1926 (charts).

In conclusion, I shall collect the various factors that have been demonstrated to act in coordination to produce in the human economy a normal balance or healthful equilibrium so that the blood plasma may contain a balanced quantity of that specific plasma protein "X." This combined calcium with the specific protein in the form here mentioned seems to present a more productive field for further research, for while the variation from normal in the free or ionized calcium and phosphorus did not prove to be definitely associated with or a cause of psoriasis, there was still evidence of a relationship of this disease to a deficiency of calcium as regulated by the parathyroid hormone. I hope in the near future to continue the work to determine the possible deficiency of the protein "X." If this can be done and means can be devised to stabilize the factor so that it may remain constant, the etiology of psoriasis should be nearer a solution and the permanent cure nearer at hand as a result of a more rational and intelligent course of therapy. The control of this deficiency must be dependent on three factors: the parathyroid hormone, the amount of serum globulin or available plasma protein of the blood that is able to combine with calcium and the supply of calcium in a form that will combine with the protein so that it may be utilized by the cells. Such diseases as tuberculosis, syphilis and other infections that invade the glands may produce psoriasis by an inhibiting influence on the parathyroid gland, and other forms of pathologic atrophy of the gland may also cause the disease by depriving the blood-forming mechanism of that part which controls the regulation of calcium content. Diseases of gastro-intestinal origin that affect the sympathetic nervous system in particular may be instrumental in producing the disease or hindering cure after other factors have been corrected. The diet may be directly responsible for the continued refractoriness of this disease, not because of the high protein content, but because of the low calcium content or calcium furnished in nonusable form. One must, then, strive to return the secretions of the parathyroid gland to normal, supply the calcium in form and quantity sufficient for the organic needs and correct such other pathologic changes as may be present and in this way aid in the formation of a normal inorganic plasma protein containing sufficient combined calcium to make impossible the formation of the scaling lesions of the disease known as psoriasis.

Dr. A. W. Stillians, head of the Department of Dermatology at Northwestern University Medical School, assisted me in the outlining of my subject for research and offered many helpful criticisms after reading the first draft of my paper. Dr. Chester Farmer, Professor of Chemistry in Northwestern Medical School, assisted in the chemical aspect of my problem. Mr. Smith Freeman gave laboratory help and assistance. Mr. D. M. Parker and Mr. Elwood Baird assisted in some of the analyses of the blood.

BACTERIOPHAGE THERAPY FOR PYODERMIA

REPORT OF TWENTY CASES *

BERNARD L. KAHN, M.D.
PHILADELPHIA

This paper is presented primarily for the purpose of bringing to the attention of physicians the fact that the use of bacteriophage is meeting undeniable success. This subject is too little known among physicians, although numerous papers concerning it have been published within the past ten years.

The story of the discovery of bacteriophage by d'Herelle [1] in 1916 follows. In August, 1916, an adult suffering from a severe form of Shiga dysentery came to the hospital of the Pasteur Institute. During the course of the patient's illness, d'Herelle made bouillon cultures of the stools daily. These cultures were incubated overnight and filtered through a Chamberland filter. A few drops of the filtrate were then added to a young bouillon culture of dysentery bacilli, and the mixture was placed in the incubator. Throughout the course of the disease, the tubes so prepared yielded normal cultures of dysentery bacilli. One morning, however, the tube prepared on the previous day was found to be sterile. At the same time it was learned that the condition of the patient had greatly improved. The sterile tube was filtered, and a few drops of the filtrate were added to a fresh suspension of dysentery bacilli and placed in the incubator. In about ten hours, this tube also became limpid. A few drops of the filtrate of this lysed culture induced complete clarification of the third suspension, and so on, indefinitely, in series. In other words, the lytic principle was regenerated with the dissolution of each culture.

When a suspension of Shiga bacilli to which a little of the filtrate had just been added was spread on an agar surface after incubation, d'Herelle noted the presence of a number of small, circular, clear areas in an otherwise uniform turf of bacterial growth. These he ascribed to the deposition of corpuscles of the lytic agent present in the mixture that had been spread on the agar surface. He believed that the original corpuscles deposited on the surface had parasitized and dissolved the growing bacteria in their immediate vicinity and that

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* From the Mount Sinai Hospital.

1. d'Herelle, F.: The Bacteriophage and Its Behavior, translated by George H. Smith, Baltimore, Williams & Wilkins Company, 1926, pp. 3-5.

the clear areas actually represented colonies of the lytic corpuscles. The number of the clear areas varied with the quality of the filtrate added to the bacterial suspension. D'Herelle concluded that the phenomenon must be due to an invisible parasite in the bacteria, and he accordingly gave it the name "bacteriophage." The phenomenon of bacterial solution caused by bacteriophage was termed bacteriophagy.

In 1921, d'Herelle published the results of a great deal of careful work covering many phases of the field opened by his original observations in his book, "The Bacteriophage and Its Behavior."

Bacteriophage, in the opinion of d'Herelle, is an ultramicroscopic organism, a filtrable virus, that is nonpathogenic for higher animal forms but specifically parasitic on various pathogenic bacteria. Other bacteriologists, including Reimann and Kolmer, consider it a bacterial enzyme. The action manifested by the bacteriophage comprises phenomena of which the final result is digestion which leads to a total dissolution of the bacterial bodies. In other words, it is a bacteriolysis.

Bacteriophagia, as defined by Alderson,[2] is a "dissolution of bacterial cells brought about by a filter passing principle which multiplies at the expense of the attacked bacteria and is therefore capable of exerting its lytic action through an indefinite number of serial passages."

The exact nature of bacteriophagia is not definitely settled, and it is not within the scope of this paper to deal with the theories that have been advanced. Let it suffice to say that as a therapeutic measure, it gives gratifying results.

In 1915, Gratia [3] described a substance capable of destroying microorganisms. In 1922, he treated about fifty patients with different staphylococcal infections and observed that the course of furunculosis, sycosis and subcutaneous abscesses was favorably influenced.

Rice and Harvey [4] used bacteriophage in fifty cases of different pyogenic conditions and obtained excellent results.

Larkum,[5] of the Michigan Department of Health, reported favorable results from treatment with bacteriophage in sixty-six cases of furunculosis.

Schultz [6] considered that d'Herelle's discovery, on account of its practical results, marked the most important epoch in the history of

2. Alderson, H. E.: The Bacteriophage in Pyogenic Infections of the Skin, Arch. Dermat. & Syph. **21**:197 (Feb.) 1930.

3. Gratia, Andre: Proc. Soc. Exper. Biol. & Med. **18**:217, 1921.

4. Rice, T. B., and Harvey, V. K.: The Therapeutic Use of Bacteriophage in Suppurative Conditions, J. Lab. & Clin. Med. **14**:1 (Oct.) 1928.

5. Larkum, N. W.: Bacteriophage in the Treatment of Furunculosis, J. Michigan M. Soc. **27**:106 (Feb.) 1928.

6. Schultz, E. W.: Bacteriophage. Its Prophylactic and Therapeutic Value, California & West. Med. **27**:481 (Oct.) 1927.

bacteriology. He considered that this discovery might lead to incalculable improvement in the treatment of patients and in checking epidemics.

Arnold [7] said:

"Bacteriophage," as used therapeutically, usually means a Berkefeld or similar filtrate of broth cultures of bacteria which have been dissolved by a lytic principle. There is present in this material the peptone and meat extractives of the broth, the dissolved bacterial proteins (probably unchanged) and a transmissible lytic principle. The protein content of the material should be borne in mind by the physician when he uses these preparations. The therapeutic effect of bacteriophage filtrates is attributed (1) to the protein of the dissolved bacteria which is in the form of a very readily available antigen, (2) to the transmissible lytic agent, which is capable of dissolving homologous bacteria, (3) to foreign protein shock when the material is injected, or (4) to a combination of the foregoing.

Whatever mechanism may be operative, it is known with certainty that, following the use of bacteriophage, the opsonic index is greatly increased and that all the antibodies that can be produced by the heat killed organisms are also produced by filtrates of bacteriophage lysed cultures.

Bacteriophage filtrates have been used most widely and with the greatest success in acute staphylococcus infections of various types.

In several cases of stubborn pyogenic conditions in which the patients presented themselves for treatment within the past year, a thorough trial of bacteriophage was started. The bacteriophage used in the reported cases was a stock product manufactured by the Swan-Myers Company of Indianapolis. This was the only product obtainable and is made after the method of d'Herelle. It is polyvalent and is sterilized by the Berkefeld filtration. No chemical preservatives are added, as the bacteriophage contains a living substance, nor must it be heated above room temperature as it may be destroyed.

The syringe to be used is sterilized by boiling and is cooled before using. Sterilization with alcohol may destroy the phage.

The twenty cases treated comprise the following conditions, and the results in each will be enumerated:

Acne, nine cases; furunculosis, five cases; hordeolum (stye), one case; alveolar abscess, one case; bed sore, one case; sycosis vulgaris, one case; ischiorectal abscess, one case, and ringworm of the toes with secondary infection, one case.

ACNE

Case 1.—G. C., a man, aged 23, a stenographer, in good general health, had a severe case of acne, with numerous papules, pustules, comedones and deep cicatrices on both sides of the face, and a few lesions on the chin, forehead and upper portion of the chest. The lesions had been present for seven years. Treatment

7. Arnold, Lloyd, University of Illinois College of Medicine: Personal communication to the author, October, 1930.

had consisted of the various local remedies generally employed for this condition, with regulation of diet and internal medication to meet indications.

On April 12, 1930, 2 cc. of staphylococcus bacteriophage was injected subcutaneously into the outer aspect of the right arm. This location was chosen because injection here is less painful than it is in any other part of the body. Since the skin was oily, local application of a sulphur lotion and ointment was ordered. The lotion was to be used twice daily and the ointment before retiring.

On April 13, there was a marked reaction at the site of injection. On April 14, the local reaction had subsided and the lesions had somewhat improved. On April 15, 3 cc. of staphylococcus bacteriophage was injected into the left arm. The reaction was mild. On April 21, the lesions were drying up, the skin was peeling and there was practically no change in the scars. On April 25, no active lesions were present, and local treatment was discontinued. On May 6, one-fourth skin unit of roentgen rays was administered to both sides of the face and forehead. On May 13, a second dose was given, on May 20 a third and on May 27 a fourth. The roentgen rays were used with the hope that the oil glands of the skin would be permanently checked in their excessive activity, and the principal cause of the condition thus be removed.

CASE 2.—V. B., a student at the University of Pennsylvania, had a severe case of acne with lesions similar to those in case 1. These lesions had been present for four years. The treatment had consisted of internal and external medications and regulation of diet.

On May 15, 1930, 1 cc. of staphylococcus bacteriophage was injected into the right arm. The same solution was also ordered for local use with the following typewritten instructions:

"Cleanse the skin thoroughly in the evening before retiring with a mild soap and lukewarm water. The skin should then be rinsed with lukewarm water and patted dry with a clean towel. Take a small pad of cotton, shake some of the bacteriophage out of the ampoule vial on the cotton and gently pat the liquid over the affected areas. This process should be repeated frequently during a ten minute period and when all of the affected skin has been treated, the preparation should be allowed to dry. The following morning, the skin may be washed as usual and cosmetics may be applied."

On May 16, there was a moderate reaction at the site of the injection, and the lesions showed reduction of their activity. On May 17, the acute lesions had practically subsided. On May 19, 2 cc. of staphylococcus bacteriophage was injected into the left arm. The reaction did not interfere with the patient's attendance at school. On May 20, the forehead was entirely clear. Several lesions still marked the nose and the side of the face. On May 21, there was noticeable improvement. On May 22, 3 cc. of staphylococcus bacteriophage was injected into the right arm. The reaction was more severe than it had been after the second injection, but when the patient was seen on May 26, the lesions had practically disappeared. The skin was smooth, and there was no apparent activity of the lesions, but the diet was still enforced. The patient was entirely cured when last seen, on May 31.

CASE 3.—N. F., a woman, aged 23, a stenographer, had a case of acne with severe lesions, of six years' duration. The condition was getting worse and had resisted all treatments, including roentgen and ultraviolet therapy.

On May 20, 1930, 2 cc. of staphylococcus bacteriophage was injected into the right arm. The same solution was also ordered for local use, once daily, with the typewritten instructions cited in case 2. On the following day there was a marked reaction. The lesions on the face were unchanged, and the temperature was normal. On May 23, the local reaction caused by the injection had subsided,

and the lesions had greatly improved. On May 24, 2 cc. of staphylococcus bacteriophage was injected into the left arm. The local reaction was not marked. The same treatment was continued locally on the face. On May 25, the lesions on the face were markedly improved. On May 27, a third injection of 2 cc. of staphylococcus bacteriophage was administered, causing a very mild reaction. The patient was seen again on May 31; the lesions were disappearing rapidly and the skin was assuming a normal appearance. On the last visit, June 23, she was entirely cured.

Case 4.—L. I., a salesgirl, aged 18, had a fairly severe case of acne which had been present for approximately four years. At one of the dispensaries she had had treatment with the usual remedies for acne. On May 23, 1930, 2 cc. of staphylococcus bacteriophage was injected into her right arm. As her skin was very oily, a solution of lotio alba was ordered for local use, twice daily, with an ointment consisting of precipitated sulphur, kaolin and zinc oxide ointment, to be applied before retiring. About nine hours after the injection, her temperature was 102 F. Her right arm was red, markedly swollen, hot and extremely painful. She was not able to work on the following day. On May 26, the acne lesions showed marked improvement. A second injection of 1 cc. of staphylococcus bacteriophage was administered into her left arm. The local reaction was not severe and did not interfere with her work. On May 31, 2 cc. of staphylococcus bacteriophage was injected into the right arm and was followed by a slight reaction. The lesions were constantly improving. On June 3, the skin had cleared, and no new lesions were present. Several ultraviolet treatments were given, and on the patient's last visit, August 12, she was discharged as cured.

Case 5.—J. M., a girl, aged 19, a stenographer, in fairly good general condition, presented a severe case of acne. She had been having these lesions constantly for about five years, and had received the usual treatment. On June 10, 1930, 2 cc. of staphylococcus bacteriophage was injected into the right arm. A sulphur lotion and a sulphur ointment to be applied before retiring were ordered for local use. On the following day, there was a fairly marked reaction, which was not severe enough, however, to interfere with the patient's work. On June 12, 2 cc. of staphylococcus bacteriophage was injected into her left arm. The local reaction was less marked than that of the previous injection. In spite of the improvement of the local lesions, the patient refused further injections. However, on June 17, 1 cc. of staphylococcus bacteriophage was again injected into her right arm, with a very mild reaction and a marked improvement in the acne. On June 24, July 1, 8 and 15, respectively, treatments with one-fourth skin unit of roentgen rays were given.

Case 6.—G. G., an automobile mechanic, aged 19, had a cardiac condition of long duration, but he was engaged professionally in wrestling and fighting. He presented a severe case of acne which he had had for about four years without receiving treatment, except home remedies. On June 16, 1930, 2 cc. of staphylococcus bacteriophage was injected into his right arm. As his skin was very oily, a modified solution of lotio alba was ordered for external use, twice daily. On June 17, the site of injection showed little reaction and pain. On June 19, 3 cc. of staphylococcus bacteriophage was injected into his left arm. On June 20, the site of injection showed a marked reaction, but it was not severe enough to interfere with his work. The lesions on his face were drying up, and on June 23, 3 cc. of staphylococcus bacteriophage was injected in his right arm. That evening there was a mild reaction, but he worked on the following day. On June 26, there were no new lesions, the skin was peeling, and the patient's condition was a great deal better. Ultraviolet irradiation was administered during the month of

July. When last seen, on August 8, the patient was well tanned, but he still showed a few scars of the previous lesions. There was at least 60 per cent improvement in the acne.

Case 7.—W. M., aged 22, a man, an usher at a theater, had had a fairly severe case of acne for five years. He had received more than twelve treatments with roentgen rays at a dermatologic dispensary as well as the usual remedies for acne and a regulated diet. On Aug. 5, 1930, 2 cc. of staphylococcus bacteriophage was injected into his right arm. The same solution was also ordered for local use, once daily, with the usual typewritten instructions. The site of injection showed the customary reaction. On August 7, the lesions were visibly improved. Again 2 cc. of staphylococcus bacteriophage was injected into the left arm and the same local medication was continued. On August 11, 3 cc. of staphylococcus bacteriophage was injected into the right arm, followed by some reaction. The pustules were fairly well healed, but several new lesions had appeared. The local application of staphylococcus bacteriophage was continued until all of the lesions had disappeared. On August 15, when the patient was again seen, the skin was smooth, and there were no new lesions. Local medication was discontinued. As roentgen treatments had already been tried, several ultraviolet treatments were given.

Case 8.—C. F., a woman, aged 26, a druggist, in fair general condition, had a severe case of acne. She had been having acne more or less constantly for about eight years; had consulted several dermatologists in Philadelphia, and had received the usual remedies for the condition. A course of ultraviolet therapy was administered, with practically no improvement. On Aug. 21, 1930, 2 cc. of staphylococcus bacteriophage was injected into her right arm. The same solution was also ordered for local use, once daily, with the customary typewritten instructions. On August 23, the site of the injection showed the usual inflammation, and the lesions on the face did not show change. Her temperature was 100.4 F. On August 25, the local reaction had subsided, and the lesions had greatly improved. A second injection of 2 cc. of staphylococcus bacteriophage was made into her left arm, with a marked reaction. The same local treatment was continued. On August 28, a third injection of 2 cc. of staphylococcus bacteriophage was administered into her right arm. On August 29, a mild reaction followed this injection, but the lesions on the face disappeared rapidly. On September 3, 10, 17 and 24, respectively, the patient was treated with one-fourth skin unit of roentgen rays on each side of the face, to smooth some of the old scars and to check the excessive activity of the oil glands.

Case 9.—M. R., a woman, aged 24, a housewife, in good general condition, presented a severe case of acne of eight years' duration. For several years, she had attended a dermatologic clinic regularly, where she had been given treatments. On Sept. 2, 1930, 2 cc. of staphylococcus bacteriophage was injected into her right arm. The same solution was ordered locally, once daily, with the customary typewritten instructions. On September 3, there was a severe local reaction, with chills and an elevation in temperature to 103 F. The right arm was painful, red and markedly swollen. The lesions remained in the same condition. On September 4, the local reaction subsided, and the pustules began to dry up. Local treatment with the bacteriophage was continued. On September 5, 2 cc. of staphylococcus bacteriophage was injected into her left arm. There was some reaction, but no fever. On September 8, when 3 cc. of staphylococcus bacteriophage was injected into her right arm, the pustular lesions on the face, forehead, nose and

chest had disappeared. The reaction to the injection this time was milder. Local treatment with the bacteriophage was continued as well as regulation of the patient's diet. Four roentgen treatments were given as a final measure.

HORDEOLUM (STYES)

CASE 10.—B. W., a woman, aged 23, a student at the Drexel Institute, in fairly good general condition, had painful styes of both eyes and pustular lesions of the face. She had been having these lesions more or less constantly for the past year, with practically no improvement. On Aug. 20, 1930, 2 cc. of staphylococcus bacteriophage was injected into her left arm. Boric acid compresses were ordered locally and calcium lactate in one-half drachm (1.94 Gm.) doses was given internally. There was a marked reaction to the injection. On August 22, 2 cc. of the bacteriophage was again injected, and the styes completely disappeared. On August 26, 2 cc. of staphylococcus bacteriophage was administered for the third time, and by August 29, all of the lesions had disappeared.

RINGWORM OF THE TOE

CASE 11.—W. V., a boy, aged 19, a musician in a motion picture theater, in good health, had ringworm of both feet, with a secondary pyogenic infection of the left little toe. A culture showed staphylococci. In order to see what effect bacteriophage would have on the secondary infection, on May 24, 1930, a wet compress of staphylococcus bacteriophage was applied locally, to be changed daily. On May 27, the pyogenic condition was entirely cured. The ringworm infection, however, persisted for several weeks until cured by a specially modified Whitfield's powder.

FURUNCULOSIS

CASE 12.—R. K., a man, aged 63, a manufacturer, suffering from angina pectoris, presented several furuncles on the back of the neck which were very painful. As he failed to improve under ordinary treatment, on April 19, 2 cc. of staphylococcus bacteriophage was injected into his right arm. The hair was removed with the following depilatory: 3 drachms (11.64 Gm.) each of powdered zinc oxide and starch and 2 drachms (7.76 Gm.) of barium sulphide. A part of this was dissolved in a small amount of water and a paste was made and applied over the neck. After a few minutes it was washed off, leaving the skin entirely free from hair. Bacteriophage-staph was used locally in the same manner as for acne. On the evening of the injection, a marked reaction developed at the site of the injection, but the intense soreness of the lesions was greatly decreased. Examination on April 21 showed that the furuncles were drying up and were less inflamed. A second injection of 2 cc. of the bacteriophage was administered into the left arm, and the same local treatment was continued. There was some reaction. When, on April 23, 2 cc. of staphylococcus bacteriophage was again injected into the right arm, the lesions were practically gone. On April 26, the patient was clinically cured of furunculosis, for there had been no recurrence of lesions up to that time.

CASE 13.—B. H., a printer, aged 32, presented eight fairly large, deep boils on both forearms. On June 3, 2 cc. of staphylococcus bacteriophage was injected into his left arm. Locally, the following ointment was applied: phenol, 4 minims (0.046 cc); mild mercurous chloride, 20 grains (1.3 Gm.); sulphonated bitumen, N.F., one-half drachm (1.94 Gm.), and rosin cerate, sufficient to make 1 ounce (29.57 cc.). The site of the injection became inflamed and was quite painful. On June 5, the lesions appeared to have dried up. A second injection of 2 cc. of

staphylococcus bacteriophage was administered into his right arm, and the same local medication was continued. The reaction was fairly moderate. On June 7, when 2 cc. of the bacteriophage was again injected into the left arm, the lesions were rapidly disappearing. When last seen, on June 14, the patient was entirely cured.

CASE 14.—E. C., a man, aged 24, a theater manager, was subject to pustular lesions on the buttocks and upper portion of the thighs. He had had this condition for several months. On Aug. 20, 1930, 2 cc. of staphylococcus bacteriophage was injected into his right arm, and wet compresses of the bacteriophage were used over the lesions locally. The site of injection was swollen, red and very painful. On August 22, 2 cc. of staphylococcus bacteriophage was again injected into the left arm. The compresses were continued locally. To prevent evaporation of the phage or its soaking into the clothes, the dressings were covered with waxed paper. The site of the injection showed some reaction. Whereas previously it had been very painful for the patient to sit, after the injection his condition was relieved to a surprising degree. On August 24, 2 cc. of staphylococcus bacteriophage was injected into the right arm; the lesions were much smaller and were gradually disappearing. On August 26, he was greatly improved, and on September 2, he was discharged as cured.

CASE 15.—G. A., a man, aged 46, a laborer, had had several large, painful boils on his neck more or less constantly for the past two years. The pain was severe enough to interfere with his work during the day and to prevent his getting proper rest at night. The ordinary remedies had failed to cure the condition.

On May 5, 1930, 2 cc. of staphylococcus bacteriophage was injected into his right arm, and after cleansing the skin with soap and water and using a depilatory for the removal of hair, the bacteriophage was used locally. There was a mild reaction at the site of the injection. On May 7, 3 cc. of the bacteriophage was injected into his left arm, followed by a very mild reaction. The lesions appeared somewhat better. On May 9, 3 cc. of staphylococcus bacteriophage was injected into his right arm. By May 12, the lesions had disappeared, although several small ones were still present on the scalp. The bacteriophage was still used locally. On May 16, new lesions appeared in spite of the treatment. A change in treatment from bacteriophage to the ointment of phenol, mild mercurous chloride, sulphonated bitumen N.F. and rosin cerate cleared the condition.

CASE 16.—J. C. B., a mechanic, aged 56, had several large furuncles over the left leg, near the knee joint. He had had this condition for several months, having used various ointments without improvement. On March 4, 1930, 2 cc. of staphylococcus bacteriophage was injected into his left arm. Bacteriophage was used locally. Examination showed that on March 7 the lesions were drying up. Two cubic centimeters of the bacteriophage was again injected into his left arm. When the patient returned for observation on March 22, the lesions had disappeared.

ISCHIORECTAL ABSCESS

CASE 17.—D. A., a man, aged 28, a clerk, presented a swelling near the anus. On Sept. 1, 1930, 2 cc. of staphylococcus bacteriophage was injected into the swelling. The reaction was mild. On September 3, 3 cc. of the bacteriophage was injected into the unopened abscess. On September 9, the abscess was incised. A considerable amount of liquid pus was evacuated. This condition healed under surgical treatment. Bacteriophage had no apparent effect, except that it probably caused a liquefication of the pus and thus hastened the recovery of the patient.

SYCOSIS VULGARIS

CASE 18.—J. R., a man, aged 63, an attendant at a swimming pool, had many superficial and deep pustules of the bearded region and the upper lip. He had been having these lesions constantly for approximately six years. On Aug. 18, 1930, 2 cc. of staphylococcus bacteriophage was injected into his right arm. A depilatory was ordered for the removal of hair, and directions were given for the local use of the bacteriophage to the bearded region. On August 20, 2 cc. of staphylococcus bacteriophage was injected into his left arm. The same treatment was continued locally. On August 22, 2 cc. of the bacteriophage was again injected into the right arm. There were no new lesions on the chin, and the old lesions were drying up. The patient left the city on August 25, with his skin distinctly improved.

BEDSORE

CASE 19.—M. C., a woman, aged 74, a diabetic patient with gangrene of the left foot, had a bedsore over the lower portion of the spine. A rubber cushion had been used to prevent pressure on the part, and various antiseptic dressings and powders had been applied, without indication of healing. On June 20, 1930, a thin layer of gauze, moistened with bacteriophage, was applied directly over the bedsore. The dressing was then covered with oiled silk to prevent it from soaking into the bed-clothes. No antiseptic was used except a daily change of dressing. In spite of the hot weather, the bedsore had completely healed by the end of July.

ALVEOLAR ABSCESS

CASE 20.—G. W., a man, aged 50, a laborer, had a tooth extracted as the result of an alveolar abscess. On Sept. 12, 1930, when he presented himself for treatment, he had a swelling at the right angle of the jaw and pain over the entire side. He was unable to open his mouth. The history pointed to necrosis of the bone and probable infection of the adjacent soft tissues, resulting in the formation of an abscess at the angle of the jaw. Two cubic centimeters of staphylococcus bacteriophage was injected directly into the lesion with a fine, sharp needle. The pain was relieved within a short time after the injection. On the following day, the redness and swelling had subsided, and he was able to open and close his mouth without pain. Because of this improvement, the patient did not return for further treatment until September 19. The swelling had reappeared, and an abscess had formed and opened of its own accord. Liquid pus oozed from the angle of the jaw. A small packing, saturated with bacteriophage, was inserted into the cavity of the abscess, and 2 cc. of staphylococcus bacteriophage was injected into his right arm. On September 22, the condition was greatly improved, and on September 27, the swelling had disappeared, and pus was not visible, but a small opening was still present. A dressing with bacteriophage was applied, and 2 cc. of the preparation was again injected into his left arm.

On October 8, when the patient returned on request, the condition was entirely cured.

COMMENT AND SUMMARY

My experience in these twenty cases, in which stock bacteriophage was given, repeats essentially the facts reported by those who have used autogenous preparations. Periods of observation after treatment have not been long enough to judge the permanency of the cures; the conditions may recur.

The significant points of this treatment are:

1. The treatment with bacteriophage seems to be a worthwhile contribution to the therapy for pyodermia.

2. It is effective even in cases in which every other treatment has failed or in which the patient apparently makes no further progress.

3. The majority of the patients received an injection of 2 cc. of staphylococcus bacteriophage every third day. To those who showed a severe reaction, 1 cc. was given. If there was no reaction or only a slight reaction after the injection of 2 cc., 3 cc. was given.

4. The results obtained with this therapy vary with the patient, the type of infection, the potency of the bacteriophage used and the thoroughness of its application. In general, the patients whose cases are reported in this article were benefited from 50 to 90 per cent.

5. Some boils were aborted. If they were well developed, their course was more rapid. The pus coming from them was liquid, and when it was evacuated, it left a clean, smooth crater, with healthy granulation tissue. Pain, as a rule, was promptly relieved, and the lesions showed diminished soreness within a few minutes to an hour after the injection or the local application of bacteriophage.

6. The foul-smelling bedsore for which this treatment was used lost its odor, became clean and proceeded to heal.

7. Lesions were promptly healed, with little induration, and thus far there have not been recurrences.

8. The use of a depilatory for the removal of matted and infected hair prevents nicking with a razor, with the resulting spread of infection.

9. When the lesions in the subcutaneous tissue were too deep to be reached by the local application of bacteriophage, an ointment containing phenol, mild mercurous oxide, sulphonated bitumen N. F. and rosin cerate was used in its place.

10. In cases of acne, when the skin was oily, the local application of sulphur instead of bacteriophage was used. Roentgen and ultraviolet therapy were used to limit the excessive secretion of the oil glands and to remove blemishes from the skin.

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Edgar B. Carter, director of the biological laboratories of the Swan-Myers Company, supplied me with more than 300 cc. of bacteriophage.

ULTRAVIOLET IRRADIATION AND AUTOHEMOTHERAPY IN LATE SYPHILIS *

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The nonspecific and particularly the chemically nonspecific treatment for late syphilis is becoming more significant, especially in cases in which the current methods of treatment are contraindicated. Among the latter are treatment by means of an infectious agent, such as malaria or rat-bite fever, and fever-producing nonspecific protein therapy. These are indicated and are the methods of choice on many occasions, giving excellent results, for example, in cases of dementia paralytica. There are, however, (1) cases in which the malarial treatment is definitely contraindicated, (2) cases that remain unchanged in spite of repeated malarial cures and (3) cases in which malarial treatment is not indicated, e. g., in tabes. One must not forget likewise that even when the infectious or nonspecific protein-produced fever is the therapeutic indication, the method is not entirely harmless and should be undertaken only in well chosen cases. Fever therapy is applicable to ambulant patients, but causes them much inconvenience. A method of treatment that is easily carried out, convenient for the patient and somewhat in the nature of a chemically specific cure and that may be repeated if necessary is not yet known. For this reason we directed our attention to the light treatment for syphilis which alone, and especially in combination with injections of autogenous blood, gave satisfactory results. Our main idea was to use the antibody-producing ability of the skin to maximum advantage. We hoped to attain this result by energetic ultraviolet irradiation. Lehner and one of us (Rajka) proved that irradiation with quartz light was more effective as a method of desensitization if it was combined with the injection of autogenous blood.

Since 1925, we have tried experimentation to obtain a scientific basis for the favorable effect of ultraviolet irradiation.

Our first results were published in 1928.[1] We treated with energetic and prolonged quartz lamp irradiations, combined with injections of

* Submitted for publication, Jan. 15, 1931.

* From the Dermatological Department of the Count Albert Apponyi Policlinic; director, Prof. Louis Török.

1. Rajka, E., and Radnai, E.: Wien. klin. Wchnschr. **41**:52, 1928.

autogenous blood, patients with late latent syphilis who gave a positive Wassermann reaction in spite of repeated and intensive chemotherapy. Later, patients with advanced syphilis of the cardiovascular and central nervous systems, some of whom had been given nonspecific therapy (milk, malaria, etc.) as well as chemotherapy, were similarly treated. As a measure of the curative effect we considered the physical state of the patients before the treatment and immediately after it, as well as the later subjective and objective clinical symptoms and the serologic and allergic state of the skin.

In the beginning we learned that too many irradiations (from fifty to sixty) may do harm. We consider thirty irradiations sufficient, after which the organism must be allowed to rest and recuperate. Generally we administered erythema doses over the whole surface of the body, in rapidly increasing amounts. In the restriction of these irradiations to a certain number, in the administration of erythema doses and in combining irradiation with injections of autogenous blood we followed the experiments of Török, Lehner and Rajka, who pointed out that every influence producing an inflammation sets nonspecific substances free which increase or diminish the inflammation. Further, the allergic organism has the ability to set special substances free that increase or weaken the inflammation (reagines and dereagines). Ultraviolet rays also have this effect. If the influencing effects (in our case the radiations) are always directed to the same place (following the depot method employed by Lehner and Rajka), the formation of weakening substances takes place with a lawful regularity. If the influence is continued after the weakening substances have appeared in the blood, the latter disappear after a certain number of treatments. Thus evidence is given of the exhaustion of the cells producing the reaction bodies. New depots must be created. As in irradiation of the entire body the whole cutaneous surface represents one depot, some time must elapse until the cells of the skin again become sensitive to ultraviolet rays, that is, until they regain their faculty of producing inflammation-weakening substances. That is why effective irradiation should always be employed intermittently.[2]

Lehner and Rajka proved that weakening substances are to be found in the largest amount in the blood half an hour after the inflammation-producing treatment. Blood taken within this optimum period can be used in the therapy. If it is taken one-half hour after ultraviolet irradiation and reinjected intragluteally or, according to our recent procedure, intracutaneously, better results will be obtained than when blood is given without preliminary irradiation.

2. Charles Brody's patients with tuberculosis were treated in the same way.

That is the reason why we introduced the injection of autogenous blood into this therapy. We do not know the reason for the favorable effect of injections of blood obtained and administered within the optimum period stated. Probably there is a stimulation of cells producing reaction bodies or a more complete outpouring of reaction bodies accumulated in the cells of the skin, that is, in the reticulo-endothelial system.

Cutaneous and intracutaneous influences, if repeated, cause a perpetual overproduction and a constantly renewed circulation of the weakening reaction bodies of the cells. These bodies attain the spirochetal foci by means of the circulation of the blood, and it depends on the permeability of the vessels (i. e., of the membranes of the central nervous system) whether the reaction bodies will have any effect. The working mechanism of ultraviolet irradiations and of intracutaneous or intragluteal injections of autogenous blood is composed of the following phases: (1) overproduction of the weakening reaction bodies, (2) an outpouring of them into the circulation, (3) their transportation to the foci of disease and (4) the attack on the spirochete.

Our present scheme of treatment is: (1) ultraviolet irradiation of the whole body with erythema doses three times a week, or thirty times in all, the therapy thus taking at least ten weeks; (2) half an hour after the first and last ten irradiations, withdrawal of blood and its reinjection in increasing doses, from 2 to 15 cc. If applied intracutaneously the blood is injected into two areas of the skin of the back, in doses of from 0.1 to 1 cc. In all, twenty injections are administered in two series, at the time of the first and the last irradiations.

We have given this treatment in sixty-two cases of syphilis: twenty-one cases of late latent syphilis without pathologic alterations of the cardiovascular and central nervous systems (congenital syphilis, one case; secondary latent, eleven; tertiary latent, nine) and forty-one cases of disease of the nervous and circulatory apparatus, among these three cases of aortitis and thirty-eight of neurosyphilis (tabes, twenty-three cases; tabes combined with aortitis, nine; tabes combined with other conditions, three; cerebral syphilis, two, and dementia paralytica, one). We purposely selected the most serious cases, with which other departments of the clinic had been unsuccessful, in order to test the effect of irradiation and injections of autogenous blood.

THE INFLUENCE ON THE WASSERMANN REACTION

Of the twenty-one patients with late latent syphilis who had a positive Wassermann reaction in spite of prolonged chemotherapy, twelve (57 per cent) gave a negative reaction following treatment. Ultraviolet irradiation and the injection of autogenous blood are, therefore, capable

of changing a positive Wassermann reaction to negative. This statement has been confirmed by Lehner. In a discussion at the International Dermatological Congress in Copenhagen, in 1930, Gottron reported similar results. The only question is how long this negative Wassermann reaction lasts. The shortest period noted by us was five months and the longest, thirty-six months. Six of twelve patients whose reaction became negative had no further treatment; the other six received from one to four courses of chemotherapy. The negative reaction produced by our therapy lasts for a longer period than that following chemotherapy, even though no subsequent treatment is given. The negative reaction is not always permanent, however; when last observed, only eight (38 per cent) of the twelve patients showed a negative reaction.

Among patients with syphilis of the central nervous and vascular systems, only those with a positive Wassermann reaction before treatment were studied as to the influence on the reaction. Of twenty-eight patients who gave a positive reaction before treatment, eight (28 per cent) gave a negative reaction following it. The change in reaction thus occurred in far fewer cases than in latent syphilis: 28 per cent as compared with 57 per cent. The duration of the negative reaction varied from two to twelve months; the patients received no subsequent chemotherapy. Four of the eight patients whose reactions became negative gave positive reactions later. Our conclusions as to syphilis of the nervous and vascular systems, are therefore the same as those regarding latent syphilis: Irradiation combined with autohemotherapy is capable of changing a positive Wassermann reaction to negative. This is true even in cases in which previous chemotherapy has had no influence on the reaction.

During the treatment a certain fluctuation was observed in the lipoid antibodies: First they increased and then they decreased. When the Wassermann test was performed at short intervals, the reaction first became stronger and then returned to its initial weakness or even became negative. This fluctuation was often found; in the cases examined, seventeen times. It seems that the first treatments caused a focal reaction in the spirochetal foci, together with a mobilization of the spirochetes. This greater activity induced an increase of the lipoid antibodies. In the following course of therapy the spirochetes diminished owing to the effect of substances reducing the inflammation. This caused the antibodies to decrease. The titer of lipoid antibodies in the blood therefore presented a regular curve.

We shall not describe the colloid reactions in detail (Darányi's reaction, speed of sedimentation of the red corpuscles); we state only that these reactions became normal owing to irradiation and that they kept this value during the following period. The refraction values of

blood serum moved along the same line. The serum refraction before the treatment was increased in almost all the patients examined: on an average, from 13540/13550 to 13476/13512 of the normal.

THE CUTANEOUS ALLERGIC RESPONSE TO LUETIN

Positive luetin reactions were obtained in forty-three cases (sixteen of latent syphilis and twenty-seven of vascular syphilis and neurosyphilis). Busson's organic luetin was used. To avoid unspecific positive reactions the luetin reaction was always read after from forty-eight to seventy-two hours.

Immediately after irradiation the reaction was increased in twenty-five cases, weakened in nineteen and unchanged in seven. A later checking of the luetin reaction showed an increase in nine cases, a weakening in sixteen and no change in three.

Without doubt, the reaction is increased after irradiation; however, this increase is to be found only when relatively few irradiations have been administered. If the irradiations are continued, the reactions become weak or anergy develops. Therefore, in the later course of observation there are more weaker than stronger reactions. One has to observe the reactions for a longer interval to obtain true values. We wish to emphasize that according to the recent investigations by Lehner and Rajka, weaker allergic reactions following increased ones are induced by anti-inflammatory dereagines. Therefore the weakened luetin reaction after increased allergic reactions is caused by dereagines. The presence of dereagines indicates a period of desensitization.

The luetin reactions in latent syphilis and in neurosyphilis are parallel. The aforementioned fluctuation of the luetin reaction is thus to be attributed less to the syphilitic alterations than to the processes due to irradiation and taking place in the skin (the fluctuations of reagines and dereagines).

The luetin reaction is not parallel with the Wassermann reaction or the colloidal reaction of the blood, but is wholly independent of them. The presence of allergy does not allow any prognostic deductions. We observed a strong luetin reaction in advanced progressive neurosyphilis and, on the other hand, a minimum or negative reaction in benign and late syphilis. In general, however, the development of cutaneous allergy is to be desired, and is a favorable symptom. Among the known antibodies in syphilis that are to be taken into consideration, only antilipoids and precipitins accompany the spirochetes, but do not destroy them. Reagines and dereagines are of greater importance, as they may be supposed to attack the spirochetes. Their production therefore seems to be a useful process. This point of view was emphasized by Nékám in his report at Copenhagen.

THE INFLUENCE ON CLINICAL SYMPTOMS

Of forty-one cases—thirty-three of tabes (pure and mixed forms), two of taboparalysis, one of dementia paralytica, two of cerebral syphilis and three of aortitis—none failed to show subjective improvement during the treatment: Ten showed distinct improvement in single symptoms, and thirty-one considerable improvement in all symptoms.

Improvement of symptoms occurred far oftener than spontaneous remissions. It was no doubt, therefore, the result of the therapy. Improvement was noted in all symptoms: the gastric crises, lancinating pains, vertigo, paresthesia, ataxic walk, incontinence of urine, etc. In the cases of paralysis the psyche became clearer. Recovery was independent of the serologic state of the patients.

The greater number of the patients were under treatment only from one-half to one year; consequently, our observations were made for a relatively short time. In only a few cases was there a longer period of observation.

THE DURATION OF IMPROVEMENT AND OCCURRENCE OF REMISSIONS

The duration of improvement was: one month in 5 cases, two months in 9 cases, three months in 5 cases, four months in 5 cases, five months in 2 cases, six months in 3 cases, seven months in 3 cases, eight months in 3 cases, nine months in 1 case, ten months in 1 case, twelve months in 3 cases, fifteen months in 1 case, eighteen months in 2 cases and nineteen months in 1 case. The improvement lasted more than a year in 7 cases, which was a remarkable result.

Recurrences occurred in nine cases; four of the patients improved after the second treatment and remained well. Relapses occurred after from two to eight months, and only five patients had a relapse after one or two courses of treatment. All the others continued to show improvement at the close of our investigations (May, 1930). If we consider that in one fifth of the cases (seven) the improvement lasted more than a year, we can suppose a longer remission in the other cases (twenty-nine). The objective symptoms showed no improvement except in a case of oculomotor paresis, in which the ptosis disappeared during the therapy.

No other nonspecific method has had a similar good effect in tabes. Hoff and Kauders, for instance, obtained no recovery in 25 per cent of patients with tabes treated by malaria.

We think that the main reason for this variation is that with the other nonspecific methods the exhausted organism of the neurosyphilitic patient is too much fatigued. The patients weakened still more by the fever cannot recover. Combined irradiation and autohemo-

therapy, on the contrary, make the patient stronger. In all cases observed, there was improvement in the general condition: the insomnia ceased and the appetite and, consequently, the weight increased (by 5 or 6 Kg.). There were greater ability to work and more vital energy; instead of going from one hospital to another, the patients began to work again.

These facts alone are sufficient for introducing ultraviolet irradiations, especially in combination with autohemotherapy, as a nonspecific treatment for cardiovascular syphilis and neurosyphilis. The easy administration, the patient remaining ambulatory, is to be emphasized. The therapy may be used as often as necessary without doing harm. It is our opinion that regular treatment given intermittently conserves the vitality of the patients and accelerates "healing" by diminishing or eliminating pain and by improving the state of health.

In our opinion it is advisable to use combined irradiation and autohemotherapy in all late cases of syphilis that are resistant to chemotherapy, i. e., nonspecific treatment, in cases in which infection or fever therapy cannot be applied and always in cases of tabes.

CONCLUSIONS

Remarkable results were obtained through general intensive ultraviolet irradiations combined with injections of autogenous blood in cases of old latent syphilis that showed positive Wassermann reaction in spite of chemotherapy, and in cases of cardiovascular syphilis and neurosyphilis (mostly tabetic) in which chemotherapy and nonspecific treatment had been employed without effect. Each treatment consisted of thirty ultraviolet irradiations and twenty injections of blood. The blood was taken half an hour after the beginning of the ultraviolet irradiation.

The positive Wassermann reaction became negative in 41 per cent of the cases (in 57 per cent of the cases of latent syphilis and in 28 per cent of those of neurosyphilis). It remained negative for from two to thirty-six months. In the later course of the illness about one half of the cases again showed a positive reaction. The colloidal reactions, and the refraction values of the serum became normal. The blood showed an increase in calcium content.

Cutaneous allergy, as determined by the luetin reaction, increased at first, but in most cases it decreased later. The decrease after the previous increase may be interpreted as a sign of desensitization.

The clinical subjective symptoms of neurosyphilis and diseases of the aorta improved in all cases (forty-one). The improvement extended to all the symptoms: gastric crises, vomiting, lancinating pains, ataxia,

incontinence of urine, etc. The duration of the remissions was from one to nineteen months. Relapses occurred in nine cases (22 per cent), of which five (12 per cent) showed no improvement on renewed treatment. During and after the treatment the patients felt and slept well, their appetite and weight increased and their ability to work and enjoy life returned. The objective symptoms, as a rule, did not show any change.

The treatment can be given easily and as often as necessary to ambulant outpatients. One must suspend the treatment, however, for certain intervals. It appears that with this intermittent treatment the improvement may be lasting.

SYPHILITIC PAROTITIS *

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The apparent rarity of parotitis as a symptom of syphilis is not the sole reason for a discussion of the subject; far more important is the fact that this condition is frequently confused with tumors in the region of the parotid. Since treatment for tumors of the parotid is largely surgical, a correct diagnosis will obviously eliminate unnecessary operative intervention. Needless surgical intervention has, as a matter of fact, been resorted to in numerous cases, as a perusal of the literature will demonstrate.

It seems unaccountable that syphilis of the parotid gland is scarcely referred to in many American textbooks dealing with syphilis. While comparatively rare, it is observed from time to time. It would appear to be less frequent at present than in former days, if one may judge from the evidence in the older literature. According to Kemp and Moore,[1] less than 0.07 per cent of syphilitic patients at Johns Hopkins Hospital had involvement of the salivary glands.

REPORT OF CASE

Primary and secondary syphilis, acute parotitis, syphilitic alopecia, rapid involution under antisyphilitic treatment.

A poorly nourished, anemic man, aged 25, was admitted to the hospital on Aug. 4, 1930. His past history was irrelevant, save for the fact that at the age of 3 he had had a severe attack of scarlet fever and since that time he had been almost deaf.

His chief complaints were a sore on the penis, a generalized eruption on the body and swelling of one side of the face. His last sexual exposure was six weeks previously. According to the patient's history, the swelling on the right side of the face had existed for about two weeks.

Examination showed two indurated lesions, the size of a pea, on the dorsum of the glans. There were a generalized, macular, erythematous eruption over the body, a typical alopecia of the motheaten variety of the scalp and a large and somewhat tender swelling in front of and below the right ear.

The inguinal, cervical and submaxillary glands were enlarged; the epitrochlear glands were not enlarged. The swelling on the face, which was in front of and

* Submitted for publication, Nov. 1, 1930.

* From the Venereal Disease Service, Department of Health, City of New York.

1. Kemp, J. E., and Moore, J. F.: Syphilis of the Salivary Glands, Arch. Dermat. & Syph. **6**:57 (July) 1922.

below the right ear, measured about 5 cm. in the horizontal and 9 cm. in the vertical diameter. It was firm on palpation, somewhat irregular on the surface and tender to the touch, with the skin over it movable, but the mass itself adherent to the deeper tissues. The skin was slightly red and appeared tense.

The subjective symptoms consisted of local pain and difficulty when the patient opened the mouth, chewed and swallowed. Phonation was interfered with, and speech was indistinct. There was moderate salivation. The patient was unable to open his mouth fully.

Examination showed the opening of Stenson's duct to be somewhat tumefied, pouting and red, but no discharge could be expressed. Dark-field examination of the penile lesions proved positive for *Spirochaeta pallida*. A Wassermann test of the blood made on the day of admission gave a strongly positive reaction (4 plus).

Appropriate antisyphilitic treatment was promptly instituted, and improvement was rapid. Within a week, pain was less marked and the mass on the right cheek was diminishing in size. Within two weeks, there was almost entire disappearance of the tumor so that no abnormality could be noted, the skin over the area being slightly wrinkled but otherwise normal. There was no pain on palpation; pain on chewing and swallowing had vanished, and there was left only a swollen and reddened orifice of Stenson's duct. There was correspondingly rapid involution of the macular eruption, and the penile sores were completely healed.

A note made on August 28 stated that the parotid area was normal in size and appearance, and that the patient experienced no pain. Up to that time the patient had received four injections of arsphenamine and five of a preparation of bismuth. It was also noted that the generalized adenopathy was diminished.

CASES FROM THE LITERATURE

The cases that appear in the literature up to 1914 are fully summarized in an article on syphilis of the salivary glands by Gerber.[2] He reviewed thirty-seven cases and gave a comprehensive historical review of syphilitic parotitis. To these we shall add the cases that have since appeared in the available literature.

Case 1.—Letulle and Vuillet [3] reported the case of a man, aged 39, who had a swelling in the region of the right cheek. It was painless, but interfered with mastication. The Wassermann reaction was strongly positive. Under treatment with iodides and arsphenamine, the lesion cleared up.

Case 2.—de Massary and Tochmann [4] described the condition of an Arab, aged 26, who had enlarged, hard, parotid glands, in whom a firm hypertrophy of the two lacrimal glands later developed. A diagnosis of mumps was rejected, and one of Mikulicz' syndrome was made. The Wassermann reaction was strongly positive. Under treatment with neoarsphenamine and mercury, rapid recovery took place in four weeks. This case was one of syphilis of the parotid and lacrimal glands.

Gundorow [5] observed three instances of syphilitic parotitis.

Case 3.—A man, aged 26, had a history of syphilis of two years' duration (chancre and generalized eruption). A bilateral parotitis developed, the tumor

2. Gerber: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1913, vol. 3, pp. 109.

3. Letulle and Vuillet: Bull. et mém. Soc. méd. d. hôp. de Paris **35**:1149, 1913.

4. de Massary, E., and Tockmann, L.: Bull. et mém. Soc. méd. d. hôp. de Paris **42**:627, 1918.

5. Gundorow: Allg. Wien. med. Ztg. **58**:449, 1913.

masses being round, smooth, the size of a hazel nut, slightly movable and firm. The skin over the masses was tense. There was slight pain on pressure. Because of the syphilitic history, antisyphilitic treatment was administered. The masses rapidly disappeared.

CASE 4.—A man, aged 43, had a history of chancre. Previous treatment had consisted of thirty mercury rubs. The patient presented himself with a recurrent roseola, enlarged lymph glands and angina. Both parotid glands were enlarged to the size of a hazelnut, and were oval, firm, movable and sharply outlined. Under the influence of mercury, the eruption and the enlargement of the glands disappeared rapidly.

CASE 5.—A student, aged 21, had superficial erosions on the prepuce. One month later the face became distorted. Both parotid glands were swollen, the left to the size of an orange and the right to that of a hazel nut. The skin over the mass was smooth, shiny and tense, but movable. The mass was somewhat lobulated. Under antisyphilitic treatment, the entire condition disappeared.

Mohr [6] observed several cases of parotitis in association with orchitis.

CASE 6.—A man, aged 36, had bilateral, symmetrical, hard, irregular swellings, the size of a pear, in the parotid region. The submaxillary, sublingual and Blandin-Nuhn glands were also enlarged. The lesions were painless. The right tibia showed a gummatous periostitis. Both testes were double the normal size. The skin over the testes was tense; the epididymis, however, was free. This case was regarded as one of bilateral parotitis in a patient with a late stage of syphilis associated with double orchitis.

CASE 7.—A man, aged 48, with carcinoma of the peritoneum, had bilateral swellings of the parotid glands and small swellings of the submaxillary and sublingual glands. Both testes were enlarged to the size of a small fist. Under treatment with mercuric salicylate, the swelling in the salivary glands as well as the testicular masses disappeared.

CASE 8.—A woman, aged 24, had bilateral swellings of the parotid, submaxillary and sublingual glands. The Wassermann reaction was negative. There was an associated thyroid dysfunction, and the patient was very obese. Under antisyphilitic treatment, the swelling in the glands disappeared, and there was a loss of adipose tissue.

CASE 9.—A boy, aged 15, with probable congenital syphilis, had bilateral swelling of all the salivary glands and an enlarged spleen. The Wassermann reaction was 3 plus. The result of treatment was not stated.

According to Mohr, every chronic enlargement of the parotid gland should be regarded as suggestive of syphilis.

CASE 10.—Guibaud [7] described the case of a woman, aged 49, who had a hard firm tumor of woody consistency in the region of the right parotid gland. The skin over this area was normal in appearance and not adherent to the mass. The Wassermann reaction of the blood was strongly positive. Five intravenous injections of neoarsphenamine caused disappearance of the tumor.

Kjellberg [8] reported two cases of syphilitic parotitis.

CASE 11.—A woman, aged 56, gave no history of syphilis. During the previous twenty years, she had had several "lumps," which had appeared over various parts

6. Mohr, L.: Ztschr. f. Geburtsh. u. Gynäk. **74**:409, 1913.
7. Guibaud: Arch. de méd. et pharm. nav. **106**:66, 1918.
8. Kjellberg: Acta dermat.-venereol. **1**:263, 1920.

of the body, ulcerated and healed spontaneously (presumably gummas). A large, firm, painless swelling developed in the region of the right parotid gland. The skin over it was reddened and warm to the touch. There was no salivation. Following treatment with potassium iodide and mercury rubs, there was marked improvement within a month.

Case 12.—A woman, aged 32, gave a history of two miscarriages. The Wassermann reaction was strongly positive. Three years later, firm, hard swellings developed in each parotid region. Under treatment with potassium iodide and arsphenamine, they diminished in size.

Case 13.—Sklarz [9] presented the case of an elderly woman, who said that she had not had a syphilitic infection. She had a swelling of the left parotid gland, as well as specific alopecia, leukoderma and a positive Wassermann reaction. After treatment with mercury inunctions and potassium iodide, the swelling of the parotid gland disappeared.

Case 14.—Simard's [10] case was that of a man, aged 74, who complained of a progressively enlarging mass in the region of the right parotid gland. It was firm and slightly adherent to the deeper tissues and the overlying skin. By exclusion, a diagnosis of gumma was made. Under antisyphilitic treatment, the lesion improved rapidly.

Case 15.—Flandin and Aubin [11] described the case of a man, aged 24, whose chief complaint was a swelling of the face which had begun seven weeks before. The right side swelled first, and the left side, four weeks later. There was no pain or interference with mastication. The skin over the swelling was normal and movable. Normal saliva was obtained from Stenson's duct. The first diagnosis was mumps, but the patient had a scar of a recently healed chancre, generalized adenopathy and a positive Hecht reaction.

Case 16.—Lemierre [12] reported the case of a man, aged 22, whose chief complaint was swelling of the face. Both parotid glands had swelled slowly and insidiously, without pain or fever. At the end of one month the patient had a left facial paralysis. Under treatment with potassium iodide, the swellings diminished and the paralysis disappeared. In three weeks the parotids had returned to normal size.

Richter [13] reported two cases of syphilis of the parotid.

Case 17.—A woman, aged 32, had a swelling of the right parotid gland of one year's duration, which later became abscessed. She complained of excessive soreness and burning in the mouth, and eventually presented an ulceration, the size of a half dollar, with undermined edges and a sharp border. The Wassermann reaction was positive. Eight injections of neoarsphenamine and fifteen of bismuth cured the patient.

Case 18.—A woman had had a syphilitic infection about twenty years before examination and had received treatment. For the past five years she had suffered from repeated attacks of inflammatory parotitis; the attacks began with the onset of menstruation, lasted from eight to fourteen days, and recurred with the next period. The diagnosis of parotid calculus was ruled out by negative

9. Sklarz: Case Presentation, Verhandl. d. Berl. Dermat. Gesellsch., May, 1922.

10. Simard: Bull. Med., Quebec **8**:67, 1906-1907.

11. Flandin and Aubin: Bull. Soc. franç. de dermat. et syph. **27**:352, 1920.

12. Lemierre, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **43**:510, 1920.

13. Richter, W.: München. med. Wchnschr. **75**:1298, 1928.

roentgen observations and by palpation. The Wassermann reaction was always negative. Because of the syphilitic history, bismuth was administered. There was improvement after three injections; after the fifteenth injection, the swellings disappeared. Six months later, the parotid swelling recurred on the left side. Further treatment with bismuth cured the patient.

Case 19.—Semon [14] described a case of bilateral parotitis in a woman, aged 54, with a history of syphilis and a positive Wassermann reaction. There was dryness of the mouth, so that solid food could be swallowed only when moistened. The salivary enzymes were absent. The patient suffered from repeated attacks of parotitis, mainly on the right side. Improvement was noted under antisyphilitic treatment.

Kemp and Moore [1] reported four cases of syphilitic involvement of the salivary glands, three of which included the parotid.

Case 20.—A Negro, aged 24, had large gummas of both parotid glands, the nasal septum and the turbinates. He had a positive Wassermann reaction. One injection of arsphenamine produced marked improvement.

Case 21.—A Negro, aged 35, had a gumma of the right parotid gland, with sinus formation, paralysis of the terminal branches of the right seventh nerve and periostitis of the right tibia. The Wassermann reaction was positive, and there was a history of syphilis.

Case 22.—A colored woman, aged 23, had a gumma of the right parotid gland, a nodular syphilid of the cheek and a gumma of the right quadriceps femoris. Following three intravenous injections of arsphenamine, all of the swellings disappeared.

Case 23.—In Mierzecki's [15] patient, a painless swelling of the submaxillary and parotid region developed two years after the appearance of an initial lesion. One year later, there was a swelling of the left testis. Roentgen treatment was unsuccessful, and for that reason the left testis was removed. Histologic examination revealed orchitis leutica. The Wassermann and Sachs-Georgi reactions were positive.

Case 24.—Jeruchimovic and Bljumkin [16] reported the case of a man, aged 42, who said that he had not had a syphilitic infection. He had a large, round, painless, immovable tumor in the region of the left parotid gland. The Meinicke reaction was weakly positive. After the administration of potassium iodide, the swelling diminished in size and the movements of the neck became easier. With further treatment, the tumor disappeared.

Case 25.—Garrahan [17] described the case of a boy, aged 15, whose complaint was a slow and progressive swelling in the region of both parotid glands. These areas were occupied by smooth, regular tumefactions of woody consistency. The masses were painless, well circumscribed and not adherent to the skin. The Wassermann reaction was positive. Under treatment with cyanide of mercury and potassium iodide, most of the tumefactions disappeared in about a month. This was a case of congenital syphilis.

Girard and Trigher [18] observed two cases of syphilitic parotitis.

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14. Semon: Proc. Roy. Soc. Med. **14**:38, 1921.
15. Mierzecki, H.: Dermat. Wchnschr. **85**:1740, 1927.
16. Jeruchimovic and Bljumkin: Vrach. dïelo **10**:1149, 1927.
17. Garrahan, J. P.: Semana méd. **1**:172, 1922.
18. Girard and Trigher: Bull. méd., Paris **40**:72, 1926.

CASE 26.—A woman, aged 24, had a maculopapular rash on the body and mucous patches in the mouth. Both parotid glands were firm and swollen. There were marked salivation, painful trismus and an elevated temperature. Rapid improvement occurred after antisyphilitic therapy.

CASE 27.—A man, aged 22, had a healed primary lesion on the penis and adenitis. A swelling developed in the parotid and submaxillary regions, with marked trismus and salivation. Rapid improvement occurred after antisyphilitic therapy.

CASE 28.—Haslund's [19] case was that of a boy, aged 8 years, with congenital syphilis. The patient came under treatment at the age of 4 weeks, with a papular eruption and coryza. The eruption disappeared following treatment with mercury. The Wassermann reaction, however, remained positive. When the child was 8 years of age, a hard, firm swelling developed on the right cheek. Despite treatment with mercury and potassium iodide, the tumor increased in size and fluctuated, leading to incision. Under further antisyphilitic treatment, the condition disappeared, which, the author stated, warrants a diagnosis of syphilis.

CASE 29.—Haslund mentioned two further cases reported in the Danish literature. The first, reported by Tage Iverson, was that of a painter, aged 45, who said that he had not had syphilis. He had a fist-sized swelling of the parotid gland, which had existed for two months, and suggestive ulcerations of the scalp, which went down to the bone. He received potassium iodide, which resulted in a partial reduction in the size of the tumor.

CASE 30.—The second case was reported by Rasch, who observed a man, aged 59, who had had syphilis for fourteen years. Two months before admission to the hospital the patient had received potassium iodide for a gumma of the hard palate. Three weeks before admission he had fever and pain on the left side of the head and swellings appeared in the parotid region which were later incised. The Wassermann reaction was positive. Under treatment with potassium iodide and mercury rubs, there was an almost complete disappearance of the lesion.

CASE 31.—A short résumé of Osler's [20] case is herewith given, since it is only mentioned in the older literature. A colored girl, aged 11, presented a symmetrical enlargement of both parotid glands. They were painless to the touch and of board-like hardness. The lobulations of the glands were readily palpable, and the orifices of Stenson's ducts were swollen. The submaxillary, sublingual and lacrimal glands were also enlarged. A nasal ulceration later developed, which was regarded as syphilitic. The administration of iodides and mercury was followed by improvement. Osler regarded this case as one of congenital syphilis, because of its course and response to antisyphilitic treatment.

COURSE AND SYMPTOMATOLOGY

The clinical picture of syphilitic parotitis permits a division into (*a*) that occurring in early syphilis, most often observed up to the end of the first year of the infection; (*b*) that occurring in late syphilis, when the process is usually gummatous, and (*c*) its occurrence in congenital syphilis, when it is observed as a late manifestation (usually after the tenth year). It appears not to have been reported in young children or infants.

19. Haslund: Dermat. Wchnschr. **62**:63, 1916.
20. Osler: Am. J. M. Sc. **115**:27, 1898.

Syphilitic parotitis by no means presents a uniform picture, for its appearance and symptomatology may be so varied as to suggest a tumor or an inflammatory process.

The duration of the infection in the early type is usually between two and twelve months. The patient is frequently weak and anemic, and may or may not present the generalized early eruption. The swelling of the parotid takes place fairly rapidly, consuming a period of several weeks. The process is more or less inflammatory, and the tumor mass is somewhat tender to the touch, reddish on the surface and tense. The lesion may attain the dimensions of a silver dollar, or even larger. It is firm to palpation, with a slightly uneven surface. The associated lymph glands are often swollen, and surround and are embedded in the parotid, adding to the tumefaction and accounting, to an extent, for the tenderness and pain which are either spontaneous or experienced on palpation. The preauricular glands are almost always enlarged. The surrounding skin may be doughy and edematous; rarely the tumor itself may be doughy, and occasionally even painful. As a rule, the swelling is bilateral and, when so, the masses are not symmetrical. Rotation of the head causes pain on the affected side. When suppuration takes place, as it occasionally does, it is usually in the lymph glands and only exceptionally in the parotid itself.

The skin over the tumors is movable, as a rule, and the mass itself is closely adherent to the underlying tissues. In this type, with the relatively rapid development of the tumor mass and the more or less acute symptoms, there is a resemblance to epidemic parotitis (mumps).

Subjective symptoms, such as salivation, pain and dysphagia, are usually marked. There is difficulty in opening the mouth, and talking, chewing and swallowing are interfered with. Fever is rare, but is occasionally observed and is common when suppuration takes place.

When syphilitic parotitis appears not associated with the early secondary manifestations (first few months), the process runs a subacute course; thus, there may be little or no redness, tenderness may or may not be present, the associated lymphadenopathy may not be so marked and the subjective symptoms may be less manifest.

In the later stages the disease develops insidiously. There is noticed a gradual increase in the size of the parotid mass. In this stage the disease is more often unilateral. Months may elapse before it is fully developed; sudden onset is therefore rare, but was reported by Fournier. Marked symptomatology can occur here as well, yet is not common. Repeated attacks of this type of parotitis have been observed. In Erler's [21] case of congenital syphilis, in which all three salivary glands were involved, there was marked swelling to the extent of producing

21. Erler, quoted by Gerber (footnote 2, p. 112).

dyspnea. Paralysis of the terminal branches of the seventh nerve has been noted by several observers.[22]

The superficial part of the swelling may become matted together and attached to the deeper tissues. The tumor mass is markedly adherent to the skin and underlying parts. Fluctuation is the next step, followed by breaking down and the formation of a sinus which in the course of time, by the extrusion of broken-down tissue, presents the clinical aspect of a gumma. Dysphagia is also often characteristic of this type. Although redness and local temperature are more frequently observed in the parotitis of early syphilis, they are occasionally encountered in the gummatous variety, as noted by Kjellberg.[8] When promptly administered, treatment results in commensurate improvement.

The insidious growth and the usual absence of marked symptomatology in the parotitis of the tertiary period of syphilis are frequently responsible for the confusion of this condition with a variety of tumors.

The parotid swelling may disappear spontaneously, but usually does so as the result of treatment. Even under treatment the gland may break down, resulting in the formation of a fistula and, at times, atrophy. Ulceration is not confined to late parotitis, since Gundorow[5] observed it in a case of early syphilis; however, this is very rare.

Under favorable conditions, the usual course of syphilitic parotitis, especially when treated, is the involution of the process through resorption and complete resolution; this may consume days or weeks, and in many instances, months, depending on whether the infection is early or late and the amount and type of treatment. A phenomenon of importance that is observed in connection with a resolving parotitis and that bears repetition is the softening and eventual suppuration of the surrounding lymph glands.

In general, the prognosis may be said to be good.

Orchitis as a complication of acute parotitis (mumps) is, of course, not unusual, and its occurrence is regarded as due to an as yet unknown relationship between the salivary and the sex glands. This phenomenon has also been observed as a complication of syphilitic parotitis, and several cases are quoted in the literature, especially by Mohr.[6] Parotitis has also been observed in relation with menstruation and pregnancy (Richter[13]).

PATHOLOGY

We have been unable to find records of the pathologic changes in early syphilitic parotitis; for obvious reasons, this type of parotitis rarely comes to biopsy or autopsy. A composite picture of the pathologic changes in later parotitis, as culled from various observers (Neumann,[23] Vuillet,[24] Gerber[2] and

22. Kjellberg (footnote 8). Lemierre (footnote 12).
23. Neumann: Syphilis, ed. 2, Vienna, Alfred Holder, 1899, p. 760.
24. Vuillet: Syphilis des glandes salivaires, Thèse, Paris, 1913.

others), presents, in brief, the following: in the salivary glands, as in other tissues affected by syphilis, there may be observed: (*a*) inflammatory interstitial fibrosis or (*b*) changes of a gummatous nature and (*c*) the two processes may co-exist.

When a section of the gland is examined grossly, it is usually found to present a striking yellow color in the center, which is surrounded by a zone of grayish transparent tissue.

Microscopically, the central portion is found to be composed of cellular detritus, which contains nuclei arranged in groups. Many small vessels are present, some being empty, others being full of a reddish-brown pigment, the whole forming a picture of granulation tissue.

In the areas adjacent to the gray substance, the tissue elements are better preserved, but there are numerous deformed cells with atrophic nuclei. The gray substance itself consists largely of granulation tissue, i.e., many well formed blood vessels with round cells and connective tissue elements. This formation of granulation tissue may be followed into the glandular parenchyma.

In some sections, particularly at the edges of the lesion, there are still recognizable remnants of the salivary glands and the blood vessels, both arterial and venous, which are the seat of thrombotic changes.

The dead tissue that surrounds the various ducts and vessels shows a fibrinous aspect, again exhibiting a close resemblance to granulation tissue. Outside these pericanalicular zones, the parenchyma of the gland itself is equally involved, yet one can easily recognize the outlines of glandular acini.

It is thus that there is a true chronic syphilitic parotitis which is characterized essentially by the formation of islands of fibrinoid necrosis (diffuse gummas) associated with specific interstitial changes. The lymph glands associated with syphilitic parotitis show either hyperplastic or gummatous changes.

DIAGNOSIS

In early syphilis no very great difficulty should be encountered in diagnosis, since other concomitant signs, such as chancre, rash, alopecia and mucous patches, will offer a clue. At the same time, acute infections, puerperal septicemia, furuncle, anthrax, temporomaxillary arthritis and acute adenitis have to be considered. According to Neumann, an important diagnostic feature is the fact that a disturbance of the local circulation does not occur in syphilitic parotitis, despite the proximity of the swelling to the large vessels of the neck. This is in contradistinction to such disturbances which do take place in acute parotitis of non-syphilitic origin.

When the disease develops later, in the secondary period, or during the tertiary period, great difficulty may be experienced in the diagnosis. In the presence of active syphilitic manifestations, such as periostitis, papulotuberculous syphiloderms and gummas, all of which have been observed in association with parotitis, the diagnosis becomes simplified. In this group, one must also consider (*a*) malignant diseases, such as lymphosarcoma, carcinoma and chondrosarcoma, (*b*) benign conditions, such as various types of cysts, myxoma, fibroma and mixed tumors, and (*c*) granulomas, such as tuberculosis, sporotrichosis and actinomycosis.

Involvement of the adjacent structures, such as gummas of the masseter muscle, should not be forgotten.

Both syphilitic and malignant tumors grow comparatively fast, a point which serves to differentiate them from benign tumors in this region; they are also immovable on the deeper tissues. The malignancies are accompanied by glandular enlargement; this is also present in early syphilis, but in the latter there are the other concomitant signs of early syphilis. Benign tumors are more circumscribed; as a rule, they are painless, not adherent and unaccompanied by glandular enlargement. As malignancy progresses, there is a marked cachexia; the tumors become adherent to the skin and the deeper structures; they are irregular in size and outline, and they show a tendency to break down. In doubtful cases biopsy will prove of service. Calculus in the duct or the gland can be ruled out by roentgen examination, palpation and sounding of the duct.

Actinomycosis attacks the parotid secondarily; the salient features here are a boardlike hardness and multiple softenings. Moreover, microscopic examination of the pus will disclose the organism. The type of sporotrichosis that comes into question is usually observed as multiple, subacute indolent nodules, which in time show the characteristic bluish color of the skin, and is accompanied by lymphangitis. The onset and course, therefore, differ from those in syphilitic parotitis. Cultures will further serve to differentiate the two diseases. There are only two cases of tuberculosis of the parotid recorded; tuberculosis will, therefore, rarely come into play in diagnosis, but it should be borne in mind. Mikulicz' disease must not be overlooked. This disease runs a very slow course, and attacks all of the salivary glands and also the lacrimal glands, which are rarely attacked by syphilis.

The Wassermann reaction is frequently negative, but this should not prejudice one against the diagnosis of syphilis. In all doubtful cases of swelling in this region, the therapeutic test should not be neglected.

Lastly, it is necessary to remember that chronic intoxications may produce parotitis, both acute and chronic. This has been observed in chronic lead poisoning by Achard, and in copper poisoning by Chauffard (quoted by Gundorow [5]). Mercurial intoxication, especially in children, and iodides are not rarely responsible for parotitis. According to Gundorow,[5] iodide parotitis is toxic and always develops in an acute form a few hours after the intake of iodides. Syphilitic parotitis is metastatic and runs a relatively much slower course. In iodide parotitis the swelling is not so hard, its outline is indistinct, it has an uneven surface and it is painful, whereas in syphilitic parotitis the tumor is hard and painless, with an irregular surface. Iodide parotitis attacks both of the parotid glands and does not suppurate. Syphilitic parotitis may or may not involve both glands, and occasionally suppurates. Enlargement of

the preauricular gland is common in syphilis and unknown in iodide parotitis. Parotitis due to iodides disappears on withdrawal of the drug and reappears on the administration of it.

CONCLUSIONS

1. Syphilis of the parotid gland is a definite clinical entity, and, while not common, it occurs with sufficient frequency to warrant attention, especially in view of the fact that it may be confounded with tumors.

2. It may occur early or late in the infection and also in congenital syphilis.

3. The early types run an acute course and are bilateral as a rule, while the later ones run a more or less chronic course and are unilateral.

4. Associated lymphadenopathy is common; the gland itself seldom breaks down. When suppuration occurs in association with parotitis, it is usually from the accompanying lymph glands.

5. Appropriate therapy is effective and frequently results in complete restitution.

6. Recognition and prompt treatment may obviate surgical intervention.

7. While parotitis early in syphilis may be readily diagnosed, the parotitis of late syphilis may offer difficulties. To be considered in differential diagnosis are a variety of tumors and the granulomas.

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UNUSUAL COLORATION OF THE SKIN AND THE MUCOUS MEMBRANE IN ARYANS*

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CASE 1.—In October, 1928, a student, aged 18, of Italian origin, consulted me at Georges polyclinic for seborrhea of the face and scalp. Careful examination disclosed that he was of great scientific interest, owing to the unusual coloration of his skin and gums.

During childhood he had had measles and diphtheria. He had smoked a great deal since the age of 15. He suffered from constipation, which sometimes lasted five days. There was nothing of importance in the heredity except that his father's brother had strikingly dark skin.

The patient was of middle height and normal constitution, and his general condition was satisfactory. The mental faculties were higher than the average. The internal organs were normal, except that systolic sounds were heard at the apex of the heart. Analysis of the urine gave normal results. There were no signs of syphilis or Addison's disease. The patient firmly refused to permit a biopsy, examination of the blood or a test of the blood pressure.

He had thick lips and disproportionately large hands and feet. The hair was crisp. On the pubes the hair-line was of a feminine type. The openings of Stenson's ducts were at the usual place, but unusual in form, being surrounded by a raised area. The color of the skin over the whole body attracted special attention; instead of being white, as is usual in Aryans, it was a bright lemon-yellow, like that of a Chinese or a Malayan. This color corresponded approximately to *N* 24 of Broca's table. The skin of the face was more suffused with the bright yellow color than the skin of other parts of the body. The color was more intense in those parts of the skin which are usually colored more strongly, as for instance the armpits and nipples. The parents stated that this color had existed since the patient's birth. He denied the possibility of its being caused by a summer insolation.

The aspect of the mucous membrane of the mouth was normal, but the color of the gums was unusual. For a distance of 3 mm. from the teeth the gum was normal; it was of a paler pink than the mucous membrane as a whole. Close to it there was a bluish-black stripe with an uneven surface. In the direction of the labial commissure the mucous membrane again acquired its normal aspect and color. Black stripes were disposed symmetrically on the upper and lower jaws, conforming to the incisors and canines; the dark color disappeared at the level of the small molars. Along the small and large molars there was a pale pink stripe, 11 mm. wide. It was on a lower level than the adjoining mucous membrane, and appeared sunken, apparently owing to the atrophy of the submucous tissue; its very distinct limits were formed by the continuation of the lines which separated the black stripe from the normal adjacent mucous membrane. Its color was paler than that of the adjacent membrane. The black stripe was 8 mm. wide and markedly separated from the normal mucous membrane by straight parallel lines on both sides; it was lower than the normal area. The intensity of its color corresponded approximately to the *N* 50 of Broca's color table. Vitro-

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pression made it less brilliant, but did not change the color. It is evident that the coloration did not result from the dilated vessels, but was due to the presence of some dyeing material in the thickness of the mucous membrane. Its surface was velvety, especially on the upper gum; it was covered with small wartlike elements the size of a poppy seed (fig. 1).

During treatment the patient was under my observation. On Feb. 10, 1929, he was shown before the Kiev Pathologo-Anatomical Society. No change had occurred in the color of the skin, but the dark stripes had become considerably lighter, the color of the upper gum growing almost normal. In April, the patient again began to smoke a great deal, and constipation appeared simultaneously. In June, the dark coloration reappeared on the upper gum and grew brighter on the lower; dark stains appeared on the sunken pale pink stripe at the level of the small molars.

One often sees persons who even in winter retain the pigmentation that they acquired during insolation in the summer. In this patient,

Fig. 1.—Bluish-black stripes on the upper and lower gingivae.

however, who was not exposed to insolation during the summer, the color of the skin clearly differed from sunburn.

Clinical examination proved clearly that this was not a case either of catarrhal or hemolytic jaundice or of pigmentation due to the ingestion of carrots or oranges (aurantiasis cutis), or to acridine or arsenic intoxication, Addison's disease, ochronosis or any other disease that produces changes in the color of the skin. The lemon-yellow tint of this patient's skin had existed from birth and was apparently a hereditary atavistic sign. The color of the skin does not depend on the color and property of the pigment itself. It is the same for all races. The intensity of the color is determined exclusively by the quantity of pigment and the way it is distributed throughout the skin. The epidermis of dark races contains more pigment than that of white races, and among the Aryans the epidermis of persons with dark hair

contains more pigment than that of light-haired persons. At the time of birth the fetus sometimes possesses no pigment or a very small quantity. In this case, owing to the crisp hair, the horizontal hair-line on the pubes, the disproportionately large hands and the other abnormalities, the atavistic origin of the coloration becomes an admissible hypothesis. Lipschütz [1] described two similar cases and quoted one of Werner's. He reported them as greatest rarities and attributed them to an atavistic return to the coloration of the ancestor of Negro origin.

It is more difficult to explain the dark color of the gums. The symmetry and regular outlines of the dark stripes as well as the variation of this heightened color are especially interesting.

At the beginning of my observation I was firmly convinced that the patient had a pigmented mole. Embryologic and clinical data did not contradict this supposition. The mucous membrane of the mouth is embryologically of the same ectodermal origin as the skin. Accordingly, it would be natural to expect that many painful processes peculiar to the skin, such as lichen planus, lupus erythematodes and nevus pigmentosus, would appear on the mucous membrane.

Bloch [2] deduced from his work that pigment may be encountered in the mucous membrane of persons belonging to the Aryan race. According to this author, Becker's recent microscopic examination proved that in the Aryan race the formation of pigment is a normal function of the mucous cells of the mouth and of the throat.

In a microscopic examination of apparently nonpigmented mucous membrane of the mouth in fifty-three autopsies, Becker [3] found melanin in the epidermis in 74 per cent of the cases and in the connective tissue in 26 per cent. He found melanin in the mucous membrane of the throat in 21 per cent. No melanin was found in the esophagus.

Reiche [4] observed pigmentation of the mucous membrane in 50 per cent of his patients who belonged to the colored races.

Fordyce,[5] in his posthumous work which dealt with diseases of the mucous membrane of the mouth and which was a summary of his observations, wrote that pigmentation of the tongue, gums and

1. Lipschütz: Ueber eine eigenartige Gelbfärbung der Haut, Dermat. Wchnschr. **83**:975, 1926.

2. Bloch: Antomie der Haut: Das Pigment, Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 1, (teil 1), p. 434.

3. Becker, S. W.: Melanin Pigmentation: A Systematic Study of the Pigment of the Human Skin and Upper Mucous Membranes, Arch. Dermat. & Syph. **16**:259 (Sept.) 1927.

4. Reiche, F.: Melanoplakia of the Mouth, abstr., Arch. Dermat. & Syph. **10**:346 (Sept.) 1924.

5. Fordyce, J. A., and McKee, G. M.: Diseases of the Oral Mucosa, Arch. Dermat. & Syph. **13**:601 (May) 1926.

other parts of the mouth is observed in white persons, especially in the natives of the Balkan countries and Far East, and in Negroes. This pigmentation, which is frequently seen in the inhabitants of the Balkan countries and of the Near East, is frequently mentioned, especially by French and American authors, and is called ethnic.

Lonjumeau [6] described a patient with pigmented spots, about 1 cm. in diameter, scattered on the mucous membrane of the lips and cheeks. He added that according to Milian all so-called ethnic pigmentation is caused by syphilis. Leukoplakia of the mouth was observed in some patients. Similar cases of melanosis and leukoplakia in the presence of syphilis were quoted by Milian and Lenormand,[7] who affirmed that pigmentation is caused by syphilis, and that it does not result from disease of the suprarenal glands. Jeanselme and Lery, in their discussion of the subject, insisted on the ethnic origin of these melanotic spots.

Milian and Launay [8] had a patient with leukoplakia and pigmentation of the mucous membrane of the mouth; he was a beggar and suffered from pediculosis; his skin was covered with scratches and pigmentation. Pautrier attributed such pigmentation of the mucous membrane to a simple transportation of the pigment from the skin, whereas Cellau attributed it to disease of the suprarenal glands, liver and spleen, sometimes provoked by syphilis.

Hudelo and Rabut [9] reported a case of pigmentation of the mucous membrane, gums, tongue, cheeks and lips, as well as of the skin and the genitalia. Apparently besides a general predisposition to the deposition of pigment, the pigmentation was caused by syphilis of the suprarenal glands and possibly also by tuberculosis.

Combes [10] had a patient with a diffuse pigmentation of the mouth lasting for twenty years; he did not succeed in establishing the etiology of the condition.

Löhe and Rosenfeld [11] called attention to the generalized pigmentation of the mouth, especially of the tongue, which is produced by bismuth intoxication due to treatment for syphilis.

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6. Lonjumeau: Leucoplasie et mélanose, Bull. Soc. franç. de dermat. et syph. **33**:134, 1926.

7. Milian and Lenormand: Leucoplasie et taches mélaniques associées sur la muqueuse buccale, Bull. Soc. franç. de dermat. et syph. **34**:401, 1927.

8. Milian and Launay: Leucoplasie et taches mélaniques buccales chez un syphilitique, Bull. Soc. franç. de dermat. et syph. **35**:125, 1928.

9. Hudelo and Rabut: Pigmentation de la muqueuse buccale, Bull. Soc. franç. de dermat. et syph. **34**:198, 1927.

10. Combes: Pigmentation of the Buccal Mucous Membrane, abstr., Arch. Dermat. & Syph. **17**:749 (May) 1928.

11. Löhe, H., and Rosenfeld, H.: The Symptom of Bismuth Poisoning in the Treatment of Syphilis, abstr., Arch. Dermat. & Syph. **17**:112 (Jan.) 1928.

Armuzzi and Strempel [12] mentioned three cases of leukoplakia and pigmentation of the mouth. They believed that in one case it was caused by syphilis and in another by chewing tobacco.

Lortat-Jacob and Solente [13] had a patient with a blackish spot on the mucous membrane of the cheek, apparently inherited from Spanish ancestors.

It is a pity that these writers, with few exceptions, did not give the exact dimensions of the pigmented parts and did not determine the intensity of the coloration, at least approximately, according to the Broca color table.

All the cases mentioned prove that pigmentation of the mucous membrane of the mouth is not rare. It appears that cases of impregnation are included in this group. The opinions of the authors as to the pathogenesis and etiology vary greatly.

Fig. 2.—Nevus vasculosus at the external corner of the eyes.

These data do not contradict my primary diagnosis of congenital pigmented mole. However, the diminution of the abnormal color, its almost total disappearance on the upper gum and its reappearance induced me to reject my first diagnosis.

It appears that the dark color of the mucous membrane depends not on the formation and accumulation of melanin, but on impregnation with some coloring substance unusual for the organism. Perhaps atrophic processes in the affected areas contribute to the accumulation of this substance. As the disappearance of the color in the gums

12. Armuzzi, G., and Strempel, R.: Melanoplakia of the Mouth, abstr., Arch. Dermat. & Syph. **11**:389 (March) 1925.

13. Lortat-Jacob and Solente: Tache pigmentaire de la muqueuse buccale chez un sujet non adissonien, Bull. Soc. franç. de dermat. et syph. **35**:303, 1928.

coincided with the period when the patient stopped smoking and its reappearance with the time that he began to smoke again, a causal connection may be established for these phenomena as in the case of Arnuzzi.[12] The diminution of color, however, occurred after regulation of the bowels, and its increase after constipation. Apparently a causal connection exists between these phenomena also. During constipation of long duration the amount of ether-sulphuric acids that are being formed is too large. Perhaps sulphuric combinations of blood and saliva and the metallic salts contained in the tobacco smoke have a reciprocal reaction. As a result, sulphuric combinations of metals are formed, fall out, permeate and dye the mucous membrane of the gums.

This is only a hypothesis that requires further investigation. The mechanism of impregnation in bismuth intoxication is analogous: The

Fig. 3.—Dark gray spots on the sclerae of both eyes.

bismuth of the blood combines with the sulphuric acid salts of the saliva, and the sulphide of bismuth which results precipitates in the thickness of the mucous membrane, forming the usual grayish-black border (Levaditi [14]).

Had the patient submitted to repeated biopsies in the beginning of the treatment and at the end of it, the pathogenesis of the disease would have been clearer. At present, one has to be satisfied with suppositional conclusions. No doubt, as in the case of Hudelo and Rabut,[9] there was a general predisposition of the tissues of ectodermal origin—that is, the skin and the mucous membrane of the mouth—to the accumulation of pigment.

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14. Levaditi: Le bismuth dans le traitement de la syphilis, Paris, Masson & Cie, 1924, p. 249.

The patient has remained under my observation. Perhaps I shall succeed later in examining more carefully the mechanism and causes of the coloration of the gums.

Case 2.—A laborer,[15] aged 28, a native of Tchernigov, came of a healthy family. The skin over the whole body of his youngest brother was dark, but it was not uniformly pigmented. On the left cheek of the patient there was a congenital nevus vasculosus. The cheek was thickened, and above and below the zygomatic region it was blue. The nevus was spreading over the upper and lower lids, as well as over the bulbar conjunctiva of the left eye (fig. 2).

The patient was tall, with a strong constitution and black hair. The skin over the whole body was dark; the color was not equally distributed but was heightened in some places. This spotted appearance was particularly to be noted on the face, chest and neck. The spots resembled chloasma. The coloration of the skin may be designated as dermatosis pigmentosa reticularis congenita.

The conjunctiva of both eyeballs was particularly interesting: Grayish-black pigmented spots of various sizes were scattered over it, occupying about two thirds of the surface (figs. 3 and 4). The sclera and iris of both eyes were also hyperpigmented. The iris and pupil were confluent and formed one round spot of

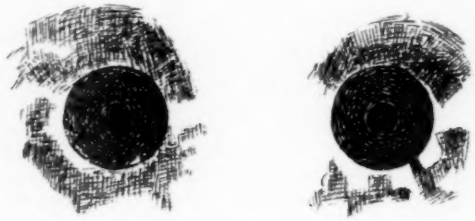

Fig. 4.—Distribution of dark-gray spots.

uniform color. For this reason it was difficult to see the contraction of the iris in testing with light.

In this case the coloration of the skin and of the forepart of the eyes was congenital: hyperpigmentatio cutis et melanosis oculi utriusque congenita.

From an embryologic point of view, the combination of an intense pigmentation of the skin with that of the eye may be explained by the ectodermal origin of the skin and the forepart of the eye.

Melanosis of both eyes is exceedingly rare. In a description of 5 cases, 4 of which occurred in white men and 1 in a Negro, Doherty[16] said that melanosis usually occurs in one eye only and is a congenital anomaly. Kubli[17] noted melanosis in only 3 of 40,000 cases.

15. The patient was shown before the Kiev Dermatological Society in March, 1929.

16. Doherty: Cases of Melanosis Oculi with Microscopic Findings, Am. J. Ophth. **10**:1 (Jan.) 1927.

17. Kubli: Melanosis oculi, Russian J. Ophth., February, 1929, p. 24.

Kubli demonstrated before the Leningrad Eye Society a patient, aged 65, who suffered from cataract and cirrhosis of the liver. A gray discoloration of the eyes began to appear at the age of 55, after prolonged injections of potassium iodide. He hesitated to determine the cause of the pigmentation, but erroneously called the condition melanosis, which is a congenital anomaly, whereas in his patient the condition appeared at the age of 55. No doubt, this case was an example of impregnation of the eye by iodized salts.

Martin [18] said that pigmented spots are to be encountered in persons belonging to races with dark skin; that the pigmentation of the conjunctival tissue of the lids is to be observed in the Javanese, and that when Aryans are crossed with Negroes the yellowish color of the conjunctival tissue and of the nail-bed of the thumb is preserved. Schwalbe and Fischer [19] called attention to the fact that in dark-skinned races the pigmentation does not stop at the limits of the mouth, anus, lids and genital parts; as in wild animals, the conjunctiva of the lids is often pigmented, and the sclerae are slightly brownish. Pigmented spots are also dispersed on the mouth.

The foregoing data refer to colored races. The pigmentation of the skin and mucous membrane that I have described is encountered only in Aryans.

SUMMARY

Both of the patients described had a congenital anomaly consisting of pigmentation of the skin and of the mucous membrane. Moreover, in case 1, a congenital atrophy of the mucous membrane of the gums was noted, as well as a predisposition to accumulate an abnormal coloring substance in the dense portions of the atrophic areas.

A familial predisposition to the formation of various pigmentary and vascular anomalies of the skin was observed in case 2.

18. Martin: Lehrbuch der Anthropologie, Jena, 1914, pp. 349 and 409.
19. Schwalbe and Fischer: Anthropologie, 1923, p. 103.

CIRCUMSCRIBED MYXEDEMA OF THE SKIN*

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The phenomenon of myxedema occurring in circumscribed areas of the skin promises to afford a means of shedding some light on the mystery of the influence of the glands of internal secretion on the skin. English and American medical literature contains but few reports of this condition, and it would seem worth while to record a case that has come under the observation of Dr. Stokes and to attempt a critical evaluation of the diagnostic criteria advanced by various investigators.

REPORT OF CASE

History.—Miss H. U., aged 36, a minister, in February, 1924, noted typical symptoms of hyperthyroidism including nervousness, precordial throbbing and palpitation, stridor and hoarseness. The basal metabolic rate was plus 55. At operation the thyroid was found to be uniformly enlarged, and a subtotal thyroidectomy was performed. The period of convalescence was stormy, and the marked hoarseness, which was noted immediately after operation, did not improve.

Bilateral paralysis of the vocal cords was recognized in August, and the patient was referred to Dr. Charles H. Frazier, who permitted us to report this case. In October, Dr. Frazier performed an anastomosis of the recurrent laryngeal and descending hypoglossal nerves. Considerable amelioration of the patient's hoarseness was subsequently noted.

At this time the patient complained of persistent drowsiness and marked loss of hair. She was given thyroid extract, 1 grain (0.065 Gm.) three times a day, and the symptoms of myxedema disappeared. For several months thereafter she took thyroid extract at irregular intervals, initiating medication for two or three weeks when symptoms were noted, then discontinuing it until they reappeared in considerable degree.

In June, 1925, two symmetrical plaques of infiltration were noted over the tibiae. Thyroid extract was not being taken at that time. The plaques soon became definitely elevated above the surrounding skin; they did not show evidence of inflammatory reaction and did not cause subjective symptoms. The patient was advised to resume ingestion of thyroid extract because of the concomitant recurrence of symptoms of myxedema. These disappeared as formerly, but no change was noted in the infiltrated plaques on the legs.

The use of thyroid extract was discontinued in September, and in December the basal metabolic rate was minus 7 per cent. The patient's weight at that time was 161 pounds (73 Kg.), or about what it was before the onset of the symptoms of hyperthyroidism. A compound solution of iodine, which was given at this

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time, produced such marked drowsiness that it was discontinued. Resumption of thyroid extract in a dosage of 2 grains (0.13 Gm.), three times a day, produced marked nervousness and tachycardia, and was suspended.

In April, 1926, a patient was seen by Dr. Stokes and, on the basis of marked similarity to several cases previously seen at the Mayo Clinic and subsequently reported by O'Leary, a tentative diagnosis of circumscribed myxedema was made. At this time the patient presented two strikingly symmetrical plaques over the anterior surface of each tibia, measuring 9 cm. in length and 7 cm. in width, definitely elevated above the surface of the surrounding skin, slightly grayish and of a tough, doughy consistency (figs. 1 and 2). General examination at this time revealed marked exophthalmos, nervousness and excitability.

Fig. 1.—Anterior view of symmetrical lesions of the plaque type of circumscribed myxedema in the pretibial region. The scar on the lesion over the right tibia is at the site of biopsy. Note the pigskin-like appearance of the surface.

Histologic Examination.—The report of Dr. Fred D. Weidman, who examined the tissue, was as follows: The piece of skin that was excised for histologic study had a slimy exterior after having been fixed in formaldehyde. Thin ropes of clear mucin could be pulled from the cut surface with forceps.

Frozen Section: The only abnormality in the epiderm was a moderate hyperplasia of prickle cells, together with a uniform lengthening of the interpapillary pegs. The acanthosis, however, was not extreme and might be regarded as secondary to pressure or other influences operating from below.

In the corium the main changes were found in the deeper parts, consisting of a marked separation of the fibro-elastic tissue. The collagen bundles and the elastic fibers were separated into individual structures in a most remarkable way. Between the fibrillae there was a finely granular, blue material traversed by occa-

sional indefinite shreds. There were also areas comprised of delicate fibrillae on which plump spindle cells were placed, i. e., newly formed connective tissue. The only remaining factor of importance was a rather dense infiltration of lymphocytes around some of the blood vessels.

Paraffin Sections: In these the epiderm was found to be comparatively normal. The most important change was the tremendous dissection of the fibers in the deeper parts of the corium; those of the papillae were not affected. The dissection was so extreme as to isolate collagen bundles and elastic fibers into individual structures. It was thought that the elastic fibrillae were hyperplastic, and that the extremely delicate fibrillar material that lay between the heavier elastic fibers was also of elastic and collagenous nature. The finely granular, blue material, such as is usually exhibited in mucoid tissue originating in the connective tissues, could not be found in these sections. The spindle cells were very rich in

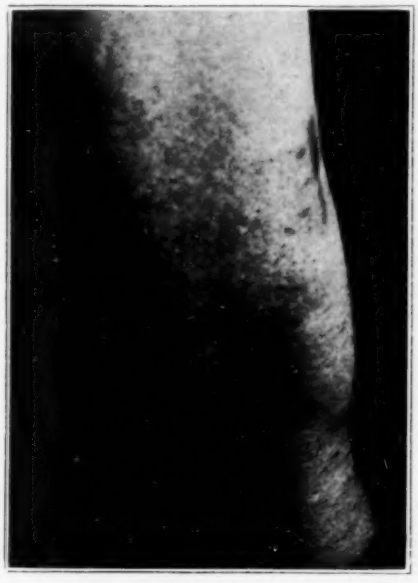

Fig. 2.—Lateral view of the lesion over the right tibia, showing elevation. The plaque is elastic, nonpitting and noninflammatory.

chromatin and stained solidly bluish black. The lining endothelial cells of the capillaries and small arterioles were likewise rich in chromatin.

In sections stained for the demonstration of mucin by the toluidine blue method of Lillie,[1] indefinite, mucinous fibrillae were visible in the corium, along with a copious infiltration of mucin in a finely granular form.

Summary.—To summarize the essential observations, this is a case of markedly toxic exophthalmic goiter in which, six months after thyroidectomy, mild symptoms of hypothyroidism intervened without producing any demonstrable changes in the skin. Following successive periods of medication with thyroid, with concomitant subsidence and intermittent recurrence of constitutional myxedema, two

1. Lillie, R. D.: A Brief Method for the Demonstration of Mucin, J. Techn. Methods **12**:120, 1929.

symmetrical plaques of infiltration were noted over the tibiae. Treatment with a compound solution of iodine and thyroid extract had no effect on the cutaneous lesions. The administration of a compound solution of iodine produced a marked increase in the symptoms of hypothyroidism, and even a slight overdosage of thyroid extract aggravated the evidences of thyrotoxicity. A recent communication from the patient indicates that the condition is undergoing the spontaneous involution reported in other cases. Histologic examination of the affected skin revealed a profound infiltration of the corium with a finely granular and indefi-

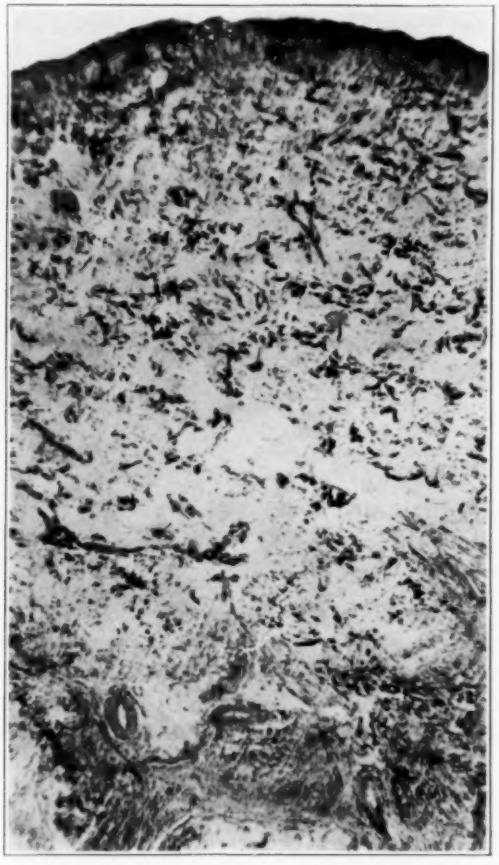

Fig. 3.—Low power view of a section, showing the general appearance of the mucoid infiltration of the corium.

nitely fibrillar substance that was demonstrated to be mucin. Other microscopic changes were an increase in the number of stellate cells and a moderate perivascular cellular infiltration.

REVIEW OF THE LITERATURE

It is a striking fact that a process arising from the derangement of a gland or glands of internal secretion should affect only certain portions of a relatively uniform organ, such as the skin. The basic

explanation of this phenomenon must lie in the demonstration of differences of physiology in the skin of various parts of the surface of the body. Little is known of the variations in function because of the meagerness of available knowledge of the physiologic chemistry of the skin.

The occurrence of myxedematous changes in isolated areas of the skin, however, has been noted by many early observers. Ord,[2] who originated the term myxedema, mentioned that the face is usually the seat of the most marked changes, often with the complete exemption of other portions. T. Kocher[3] cited two cases in which, following thyroidectomy, nonpitting edema of the legs was an outstanding feature. A. Kocher,[4] in his comprehensive monograph on exophthalmic goiter, mentioned the not uncommon occurrence of thickening of the skin and stated that it was most inclined to occur on the lower extremities.

The first specific reference to the syndrome, of which our case is an example, is found in a case reported by Hektoen[5] in which there occurred bilateral, circumscribed, mucinous infiltrates of the legs in association with exophthalmic goiter. In 1899, Morrow[6] cited a case of generalized myxedema in which there was rapid improvement under treatment with thyroid extract. Later, however, marked signs and symptoms of exophthalmic goiter developed, and coincidentally there were noted symmetrical, raised areas of swelling on the legs, sharply circumscribed, beginning 2 inches (5 cm.) above the ankles and extending upward for 7 inches (17.78 cm.).

Dubreuilh[7] was the first writer to describe a case of myxedematous nodular infiltration of the skin unassociated with exophthalmic goiter. He termed the condition "fibromes miliaires folliculaires" or "sclérodermie consécutive," and believed that the case was one of early scleroderma. The histologic picture, however, was that of myxedema.

Reitmann[8] later described a case of nodular infiltration of the skin, which histologically resembled myxedema. The face and palate showed changes which were interpreted as scleroderma. In sections taken

2. Ord, W. M.: Myxedema and Allied Disorders, Brit. M. J. **2**:1473, 1898.

3. Kocher, T.: Ueber Kropfexstirpation und ihre Folgen, Arch. f. klin. Chir. **29**:254, 1883.

4. Kocher, A.: Ueber Morbus Basedowii, in Kraus and Brugsch: Spezielle Pathologie und Therapie innerer Krankheiten, Berlin, Urban & Schwarzenberg, 1919, vol. 1, p. 751.

5. Hektoen, L., cited by Watson-Williams, P.: Clin. J. **7**:93, 1895.

6. Morrow, Howard: Symmetrical Areas of Solid Edema Occurring in Graves' Disease, Brit. J. Dermat. **40**:286, 1899.

7. Dubreuilh, W.: Fibromes miliaires folliculaires; scléroderme consécutive, Ann. de dermat. et syph. **7**:569, 1906.

8. Reitmann, K.: Ueber eine eigenartige der Skleroderme-nahestehende Affektion, Arch. f. Dermat. u. Syph. **92**:417, 1908.

from the nodules over the body there were visible merely a marked mucinous infiltration, little cellular deposition and practically no hyperplasia of the connective tissue. His interpretation of the case was the same as that offered by Dubreuilh, namely, that it was a condition midway between scleroderma and myxedema.

Von Lewtschenkow [9] was the first observer to point out definitely the myxedematous nature of the condition. He reported a case of nodular swellings of the fingers, forearms and face of a woman, aged 36, in which the onset of the process was accompanied by fever, general malaise and headache. Typical diffuse myxedematous swelling of the face and eyelids was also noted. Histologically, the lesions presented the most pronounced changes in the pars reticularis; there was marked mucinous infiltration with separation of the fibers of the cutis and a profusion of spindle cells. In 1912, Pellizzari [10] reported a somewhat similar case which he termed myxomatosis nodosa.

In 1916, Dössekker [11] made his classic description of the condition which he termed atypical tuberous myxedema, and in which he demonstrated definitely its relation to the pathologic changes of the skin in generalized myxedema. Since Dössekker's report, cases have been cited by Hoffmann,[12] Pawloff,[13] Goldenberg,[14] Bogroff and Krupnikoff,[15] Per and Rossiansky,[16] Samek,[17] Richter [18] and O'Leary.[19]

For lucidity and ease of comparison, we have classified the essential features of previously reported cases in the accompanying table. Details in such a table must of necessity be meager, but we shall attempt a

9. von Lewtschenkow, D. D.: Ein seltener Fall von myxomatösen Hautdegeneration, Monatsh. f. prakt. Dermat. **60**:239, 1912.

10. Pellizzari: Ein Fall von Myxomatosis nodosa, Arch. f. Dermat. u. Syph. **112**:7, 1912.

11. Dössekker, W.: Ueber einen Fall von atypischem tuberösem Myxödem, Arch. f. Dermat. u. Syph. **123**:76, 1916.

12. Hoffmann, Heinrich: Ueber zirkumscriptes planes Myxödem, mit Bemerkungen über Schleim und Kalk bei Poikilodermie und Sklerodermie, Arch. f. Dermat. u. Syph. **146**:89, 1923.

13. Pawloff, P.: Ein Fall von atypischem tuberösem Myxödem, Arch. f. Dermat. u. Syph. **147**:513, 1925.

14. Goldenberg: Case Presentation, J. Cutan. Dis. **34**:387, 1916.

15. Bogroff, S. L., and Krupnikoff, D. P.: Zur Klinik der Hautdysthyreose, Arch. f. Dermat. u. Syph. **147**:61, 1924.

16. Per, M. I., and Rossiansky, N. L.: Ein Beitrag zur Frage des atypischem tuberösen Myxödems (Jadassohn-Dössekker), Arch. f. Dermat. u. Syph. **156**: 320, 1928.

17. Samek, J.: Ueber zirkumscriptes Myxödem, Dermat. Wchnschr. **87**:1607, 1928.

18. Richter, W.: Ueber lokales Myxödem der Haut, mit Beziehung zum Basedow, Dermat. Wchnschr. **84**:51, 1927.

19. O'Leary, Paul A.: Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter, Arch. Dermat. & Syph. **21**:57 (Jan.) 1930.

fuller delineation of the points of similarity and dissimilarity in the subsequent discussion. The cases of Dubreuilh and Pellizzari are included in the outline for purposes of historical accuracy, but are not considered in the discussion because of the incomplete data at hand concerning them.

ANALYSIS OF THE MATERIAL TABULATED

Age.—Of the twelve patients considered, three were in the third decade of life, four in the fourth, two in the fifth, two in the sixth and one in the seventh. Obviously, conclusions as to age incidence cannot be drawn from such a small series, but the tendency is toward that shown in a tabulation of age incidence in ninety-six cases of generalized myxedema reported by Hun and Prudden.[20] In their series, 15 per cent were in the third decade of life, 30 per cent in the fourth, 25 per cent in the fifth and 15 per cent in the sixth.

General Symptoms.—One is struck by the fact that in all the reported cases of circumscribed myxedema, the general symptoms of weakness, sluggishness, unsteady gait, subnormal temperature and lowered metabolic rate are moderate or entirely absent. The metabolic rate, certainly the most acceptable evidence of hypofunction of the thyroid gland, is reported in eleven cases. In three of these the rate was not above normal, and in O'Leary's cases the readings varied between plus 21 and plus 51 per cent.

In our case the pretibial plaques appeared following a period of several months during which symptoms of hypothyroidism were unmistakably predominant. The patient complained of persistent drowsiness and noticeable loss of hair; these symptoms always disappeared following ingestion of thyroid extract. There can be no doubt that the onset of the circumscribed myxedema was in immediate association with general symptoms of hypothyroidism.

Pathologic Observations.—It will be noted that the histologic changes in the reported cases are remarkably constant. Indeed this feature is the only observation that is in relatively complete agreement throughout the entire series. Dössekker stated that the epiderm was essentially normal and did not show the atrophy caused by pressure that one might expect. He found only a moderate mucinous degeneration of the papillae and of the upper layers of the corium. In the lower portions, however, throughout the whole cutaneous network, there was a marked infiltration of a blue material which he considered mucin and in which indefinite shreds could be made out. There was marked vacuolization, and the elastic and collagen fibers were so separated and displaced

20. Hun, Henry; and Prudden, T. Michell: Myxedema, Am. J. M. Sc. **95**: 140, 1888.

Twenty-Two Cases of Circumscribed Myxedema of the Skin Described in the Literature

Reported by	Age, Sex	Type	Distribution	General Symptoms	Pathologic Process	Treatment and Result
Hektoen..... 1895	..	Plaques	Pretibial	Exophthalmic goiter		
Morrow..... 1899	♀	Plaques	Pretibial	Myxedema, followed by exophthalmic goiter	.....	No improvement under treatment with thyroid
Dubreuilh..... 1906	..	Nodular	Trunk and extremities	None	Mucinous infiltration of corium	
Reitmann..... 1908	40 ♂	Nodular	Arms, face and legs	Typical scleroderma of mouth, buccal cavity and pharynx	Mucinous infiltration of corium, with rather marked production of connective tissue	
von Lewtschenkow..... 1910	36 ♀	Nodular and diffuse	Fingers, forearms and face	Onset with symptoms of general infection	Mucinous "network" in pars reticularis	No change under administration of mercury and calcium; somewhat improved with use of iodides
Pellizzari..... 1912	..	.....	.....	.....	Details not available; case of "myxomatosis nodosa"	
Dössekker..... 1916	51 ♂	Nodular, with diffuse infiltration of face	Face, ears, hands, back and scrotum	Headache	Changes entirely in cutis; blue, shredded, infiltrating mass; vacuolization; a "strange unusual fungus-like" appearance; some lymphocytic infiltration	No change with administration of arsphenamine, potassium iodide, fibrolysin, thorium-x or thyroid extract; steady involution following implantation of thyroid in muscle; death from supposed intercurrent infection after 5½ months
Goldenberg..... 1916	?	Diffuse and nodular	Hands, forearms, upper part of back, hips, knees and feet	Malaise; diarrhea	Myxomatous degeneration of corium	Marked improvement under treatment with thyroid
Bogroff and Krupnikoff. 1924	61 ♀	Nodules and plaques	Upper part of back, extensors of arms, buttocks and knees (localized over nerve trunks)	None	Mucous degeneration of corium	?
O'Leary..... (8 cases) 1930	23	Infiltrated, tawny plaques	Over both tibiae	Recurrent, acute hyperthyroidism; rate, plus 21 basal metabolic	Major changes in cutis; thickening; mucin in masses and in strands; short strands of collagen; edema and homogenization of connective tissue fibers; oval and stellate cells scattered throughout	No change following ingestion of iodine; plaques excised; keloid formation in scars; no recurrence

	56	Infiltrated, tawny plaques	Over both tibiae	Recurrent, acute hyperthyroidism; basal metabolic rate, plus 30%	The same as in the previous case with a slight tendency to inflammatory reaction	No change following ingestion of iodine, and injection of thyroxin intravenously
		Small nodules	Legs	Basal metabolic rate, plus 52%; history of tuberculous lymph nodes, pulmonary tuberculosis, erythema induratum and papulonecrotic tuberculids	No biopsy	
	30	Infiltrated, tawny plaques	Over both tibiae	Onset of hyperthyroidism after lesions of the skin had developed	Not noted	Gradual incomplete involution following thyroidectomy
	Ages not given	Infiltrated, tawny plaques (four cases)	Over both tibiae	Recurrent, acute hyperthyroidism	Not noted	Two cases involuted spontaneously
Hoffmann..... 1923	32 ♂	Diffuse, nodular lichen-Vidal-like patch	Typical myxedema of face; lichen-Vidal on right hand; nodules on forearm	Zondek's electrocardiographic phenomenon	Marked mucinous infiltration of corium; skin from back normal	Complete involution when treated with thyroidin
Pawloff..... 1925	36 ♀	Nodular and diffuse	Diffuse thickening on face; nodules on upper part of chest, on neck and upper portion of arms	None	Moderate lymphocytic infiltration; mucinous separation of collagen and elastic fibers; numerous spindle and stellate cells	
Richter..... 1927	25 ♂	Infiltrated plaques; symmetrical	Over lower third of both tibiae	Preceding symptoms of exophthalmic goiter; onset of plaques following partial thyroidectomy	Marked looseness and paleness of corium; mucin; numerous stellate cells	Death following complete thyroidectomy; enlarged thymus at autopsy
Samek..... 1928	..	Infiltrated symmetrical plaques	Over both tibiae	Followed exophthalmic goiter	Mucinous separation of fibers of corium; stellate cells; some lymphocytic infiltration	No result with thyroid extract
Per and Rossiansky..... 1928	42 ♂	Nodules	Scalp, face, left shoulder and arm, buttocks, sacral region, abdomen, left popliteal space and calves	Basal metabolic rate, minus 3% (Krogh)	Surface of cut tissue mucinous; infiltration of mucin in corium; mast cells; thyroid of colloid type	Use of thyroid extract, potassium iodide, testicular extract and pituitary extract gave no result; gradual involution following implantation of extraneous thyroid gland in muscle and transplantation of lingual artery to thyroid gland

by the mucinous infiltrate as to lend a most bizarre fungus-like appearance to the whole section. He noted a moderate lymphocytic infiltration.

Pawloff, von Lewtschenkow, Richter and Per and Rossiansky stressed the large number of stellate cells present in sections from their cases. Cells of this type were especially numerous in our sections, scattered about in areas in which delicate fibrillae of newly formed connective tissue could be discerned. This relative increase in the number of immature connective tissue cells would seem to indicate that some agent was acting to retard their development to the mature form. If this increase were regarded as evidence of some agent stimulating the development of more stellate cells, one would expect to find a corresponding increase in the number of mature forms. Such is not the case, and it must be concluded that the stimulus that normally promotes the evolution of these cells is lacking. Support for such an interpretation is found in a theory advanced by Ribbert,[21] who expressed the belief that in thyroid disease the fibroblasts undergo changes and come to resemble embryonal "star cells." He expressed the opinion that the secretion of the thyroid is a large factor in the development and differentiation of the collagen network; this theory has been offered as an explanation of scleroderma.

The most marked and constant feature of the histologic changes in all reported cases of circumscribed myxedema is the presence of large amounts of a mucinous network in the cutis. Dössekker reviewed the literature concerning the presence of mucin in myxedematous skin and concluded that it is an almost constant sign in cases in which the process is well advanced. Ord mentioned the presence of large amounts of mucin in the skin of patients with diffuse myxedema, but did not consider it a constant observation. Unna[22] stated that he could demonstrate mucin in myxedema consistently by the use of polychromatic methylene blue (methylthionine chloride, U. S. P.). Virchow[23] and Beck[24] did not regard mucinous infiltration as a constant sign in myxedema, and they mentioned a moderate degree of atrophy of the fat. Virchow stated that he could not regard the process as a passive one, i. e., merely a deposition of mucin without the intermediation of the tissue involved. The hyperplasia of the elastic tissue and the perivascular infiltration evident in our sections would seem to substantiate this view.

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21. Ribbert, H.: Ueber das Myxome, Frankfurt. Ztschr. f. Path. **4**:30, 1910.

22. Unna, P. G.: Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894, vol. 29, p. 1004; also in Orth: Lehrbuch der speciellen pathologischen Anatomie, Berlin, A. Hirschwald, pt. 2, 8 Lfg.

23. Virchow, R.: Myxödem, Berl. klin. Wchnschr. **24**:120, 1887.

24. Beck, C.: Ueber die histologischen Veränderungen der Haut bei Myxödem, Monatsh. f. prakt. Dermat. **24**:597, 1897.

Rather convincing evidence of the presence of mucin in the skin as a constant observation in myxedema is found in the work of Schlagenhaufer and von Jauregg,[25] who noted in cretinoid dogs a sharply defined, clear blue substance intertwining among the fibers of the collagen network in sections of the skin stained with hematoxylin-eosin. Following feedings of thyroid the blue-staining mass disappeared, coincident with improvement of the general symptoms. A similar picture was found in thyroidectomized animals, the changes always being most marked in the cutis. Horsley [26] described a "gelatinous infiltrate" in the cutis of sheep on which thyroidectomy had been performed, and he was able to demonstrate the mucinous nature of this substance.

The origin of the mucinous infiltrate offers an interesting field for speculation, but little information as to the exact mechanism of its deposition is available. It is difficult to conceive of such a process occurring in isolated areas without some specific intermediation of the tissues involved. Dössekker, von Lewtschenkow, Pawloff and Per and Rossiansky expressed the belief that there is little degeneration of the structures of the cutis. In fact, Per and Rossiansky stated that the histologic observations consist of "nothing more than normal skin in which a marked mucinous infiltration has taken place." Our observations do not substantiate this view entirely. There was definite evidence of moderate degenerative changes in the elastic fibers, as shown by their basic color. The rather unusual quantities of elastic tissue and, furthermore, elastic tissue that was of such an unusually delicate structure, stimulated the suspicion that the mucin in this case was a derivative of elastin.

In Richter's case of circumscribed myxedematous plaques over both tibiae following thyroidectomy for exophthalmic goiter, marked hyperplasia of the thymus was found at autopsy. Richter expressed the belief that the changes in the skin must be explained on the basis of generalized dysfunction of the endocrine system induced by the toxic state, rather than as a result merely of hypothyroidism. He stated, however, that the histologic changes are typically those of myxedema.

There can be no doubt that dysfunction of the thyroid is frequently accompanied by disturbances of other glands of internal secretion that may influence the skin. Anders,[27] in his statistical study of myxedema in the United States and Canada, considered the association of hypo-

25. Schlagenhaufer, F., and von Jauregg, W.: Beiträge zur Aetiologie und Pathologie des endemischen Kretinismus, Leipzig, 1910.

26. Horsley, V.: Die Funktion der Schilddrüse, Festschrift für Virchow, 1891; cited by Dössekker (footnote 11).

27. Anders, J. M.: Myxedema and Cretinism in the United States and Canada, Contrib. Med. & Biol. Research **1**:280, 1919.

thyroidism and other endocrine dysfunction not uncommon, reporting Addison's disease in one and pituitary disease in two of fifty-five cases summarized. Janney and Isaacson [28] showed that, following thyroidectomy, hypoglycemia and a delayed sugar tolerance curve occur. Wilder [29] reported that diabetes was found in 1.1 per cent of his cases of hyperthyroidism, and he pointed out the marked tendency of hyperthyroidism to fan diabetes into flame. He also stated that myxedema is markedly palliative to diabetes and concluded that there is no specific interdependence of the thyroid and pancreas and that the relation is only an apparent one because of the marked influence the thyroid exerts on the general metabolism of the body. Good and Ellis [30] reported a case of myxedema associated with enlargement of the pituitary gland. Sergent [31] described a case in which myxedema followed destruction of the testes by a wound resulting from a gunshot. A. Kocher [32] expressed the belief that an enlarged thymus is found in from 40 to 50 per cent of all cases of exophthalmic goiter. Riesman [33] admitted the frequency of an enlarged thymus, but believed it unlikely that it plays an important part in the symptom complex of exophthalmic goiter.

Numerous similarly suggestive cases, of which the foregoing are typical examples, are found in the literature. They point conclusively to the frequent occurrence of simultaneous disturbance of two or more glands of the endocrine system, but no logical explanation of the mechanism is forthcoming. If Richter's explanation of the formation of myxedematous plaques in exophthalmic goiter, that they are the result of local hypothyroidism secondary to disturbances in other glands of internal secretion, is to be accepted, it is difficult to see why this complication should not be more commonly encountered in view of the frequent association of exophthalmic goiter with disturbance of the rest of the endocrine system.

Types of Lesions and Distribution.—Samek expressed the belief that the changes in the skin in myxedema may be divided into three types: (1) myxedema diffusum, the common form, (2) myxedema tuberosum and (3) myxedema papulatum. We have found only one case of the

28. Janney, N. W., and Isaacson, V. I.: The Blood Sugar in Thyroid and Other Endocrine Diseases, Arch. Int. Med. **22**:160 (Aug.) 1918.

29. Wilder, R. M.: Hyperthyroidism, Myxedema, and Diabetes, Arch. Int. Med. **38**:736 (Dec.) 1926.

30. Good, W. H., and Ellis, A. G.: Myxedema with Tumor of Pituitary Body and Lesions of Other Endocrine Organs, Endocrinology **2**:431, 1918.

31. Sergent, E.: Connection of Attenuated Myxedema with Ovarian or Testicular Insufficiency, Rev. franç. d'endocrinol. **3**:154, 1925.

32. Kocher, A.: Ueber Basedow'sche Krankheit und Thymus, Arch. f. klin. Chir. **105**:924, 1914.

33. Riesman, D.: Thymus and Status Thymolymphaticus, in Oxford Medicine, London, Oxford University Press, 1929, vol. 4, p. 50.

latter recorded, that of Hoffmann, in which a typical lichen-Vidal eruption on the right hand was noted in conjunction with a diffuse myxedematous infiltration of the face and nodules on the forearm. In this case, one of the nodular lesions showed the typical mucinous infiltration common to all the cases in this series, and the entire picture became normal following administration of thyroid extract. The evidence for considering the lichen-Vidal-like process on the hand in Hoffmann's case as myxedematous, however, is but fragmentary.

A cursory glance at the accompanying table reveals the fact that the cases tabulated fall into two distinct groups; (1) those characterized by nodular infiltrations variously distributed to the face, arms, back and scrotum, and (2) those in which are found plaques limited to the pretibial areas and in which the development of the manifestations of the skin is invariably associated with exophthalmic goiter. The local histologic changes are the only consistent point of similarity between the two groups, and these changes, so far as we have been able to determine from the several detailed descriptions published, are identical.

Of twenty-three cases considered in this regard, ten were of the nodular variety and thirteen were similar to our case, namely, pretibial plaques associated with exophthalmic goiter. All but one case of the nodular type were associated with diffuse myxedematous infiltration of other portions of the body, particularly the face.

Positive evidence that the nodular type of circumscribed myxedema is not an accompaniment of exophthalmic goiter is found in the carefully studied case reported by Per and Rossiansky. In this instance, implantation of the lingual artery in the thyroid gland was performed. At operation a small piece of thyroid tissue was removed, and histologic examination revealed a typical simple colloid structure.

Differential Diagnosis.—Because of the decided suggestion of a leonine facies in many of the reported cases of circumscribed myxedema, several investigators have searched carefully but unsuccessfully for Hansen's bacilli in nasal smears and in the skin. The clinical and histologic picture, together with reports of cure under appropriate medication in the nodular variety, seems to rule out a diagnosis of elephantiasis. O'Leary reported repeated negative examinations for *Filaria sanguinis-hominis.* Lymphedema presents a microscopic picture somewhat similar to myxedema, but there is a much more marked proliferation of the connective tissue; the endothelial lining of the lymph spaces can be made out, and there is usually a more distinct inflammatory reaction.

The differentiation of scleroderma from circumscribed myxedema presents a much more difficult problem. Early observers, such as Reitmann and Dubreuilh, regarded myxedema as atypical scleroderma.

They remarked, however, that the histologic picture differs markedly from scleroderma, which presents a more profuse infiltration of the connective tissue, pronounced atrophic changes in the cutis and a more definitely inflammatory reaction. Hoffmann stated that mucin is demonstrable in small amounts in scleroderma, as well as in poikiloderma and acrodermatitis atrophicans, and he remarked on this constant sign in what he considered known endocrine disorders. The mucinous infiltration is, however, much more pronounced in myxedema than in the other conditions mentioned.

The closeness with which myxedema may be related to other conditions is seen in a case reported by Drouet [34] of myxedema in a young girl, in which typical epidermolysis bullosa and scleroderma intervened; and a case of exophthalmic goiter reported by Vallery-Radot, Hillemand and Chomereau-Lamotte,[35] in which myxedema and generalized scleroderma occurred progressively, a striking instance of successive changes apparently initiated by dysfunction of the thyroid gland.

O'Leary, without specific reference, was inclined to doubt the validity of the diagnostic criteria in some cases of circumscribed myxedema of the face and the upper part of the chest. Details are lacking in many of the reported cases, but in the reports of Dössekker, Pawloff and Per and Rossiansky the differential diagnosis and the details of study are so comprehensive as to make skepticism difficult. We feel that on the basis of these reports nodular localized myxedema may be accepted as an entity.

Results of Treatment.—Of five cases of the nodular type of circumscribed myxedema, two responded favorably to thyroid extract; in one, some involution was noted following the administration of iodides, and in two, gradual improvement followed implantation of colloid thyroid tissue in muscle. Arsphenamine, fibrolysin, thorium-x, testicular extract and pituitary extract were variously tried without result. In twelve cases of myxedematous plaques associated with exophthalmic goiter, including our own case, no change was noted with the use of thyroid extract or iodine, and in Samek's case no change followed the implantation of thyroid in the pectoralis muscle.

It will be noted in our case that ingestion of iodides was followed by aggravation of the symptoms of hypothyroidism, whereas very moderate excess in the dosage of thyroid extract produced toxic symptoms. A parallel of this condition is found in a case reported by

34. Drouet, L.: Endocrinides cutanées (sclérodermie, épidermolyse bulleuse) chez un myxoedemateux, Bull. Soc. franç. de dermat. et syph. **35**:503, 1928.

35. Vallery-Radot, P.; Hillemand, P., and Chomereau-Lamotte, B.: Maladie de Basedow, myxoedème, puis sclérodermie generalisée, avec état sclérodermique du voile du palais, Bull. et mém. Soc. med. d. hôp. de Paris **50**:1149, 1926.

Haines [36] in which, following thyroidectomy, swelling of the face was noted together with persistence of the symptoms of hyperthyroidism. Administration of iodides produced evidences of myxedema, and the use of thyroid extract heightened the symptoms of exophthalmic goiter. Iodine and thyroid extract given simultaneously produced amelioration of all the symptoms. Haines concluded that this illustrated a condition in which the thyroid was producing no normal secretion, and when the toxic secretion was "neutralized" by iodine, the patient became myxedematous.

COMMENT

In the reported cases, the only attempt at an explanation of the etiology of the condition is Richter's suggestion that it is dependent on a general dysfunction of the entire endocrine system, induced by hyperthyroidism.

In all cases of the plaque type, it is noticeable that the area affected is remarkably constant, namely, the lower portion of the legs. Only one other suggestion of another site of involvement is found, and that is in some of Basedow's [37] early cases, in which he wrote of the "kolossal dick" skin of the abdomen. It would seem that this predilection for a certain area must have some significance. Possibly the circulatory stasis of the legs so commonly observed in cases of exophthalmic goiter may change the usually easily reversible condition of myxedema into a resistant, almost irreversible process. Administration of thyroid extract might then, instead of quickly causing the myxedema to vanish, merely aggravate the circulatory embarrassment which was a potent agent in the original development of the lesions. In all of O'Leary's cases, long-standing edema of the extremities of cardiac origin was a feature.

As has been previously noted, our case apparently was one in which the amount of normal secretion of the thyroid gland was greatly reduced, and practically all of the secretion was toxic. As in the case cited by Haines, there was in reality a deficiency of thyroid in a person with a toxic condition of the system. One may easily conceive of a myxedematous condition of the skin in the presence of a toxic state of the organism as a whole. Numerous reports of diffuse myxedema in connection with exophthalmic goiter seem to indicate that this may be the case.

O'Leary was reluctant to use the term myxedema in connection with his cases, because he believed that the term had come to denote the entire group of constitutional symptoms following hypofunction of the thyroid gland, and he considered the cutaneous changes a minor part

36. Haines, S. F.: Exophthalmic Goiter and Myxedema: Report of a Case, Endocrinology **12**:55, 1928.

37. Basedow, cited by Morrow (footnote 6).

of the picture. He also pointed out the questionable evidence of myxedema in most of the cases. It should be remembered, however, that myxedema (mucin edema) is among the most apt terms in all medical literature for the peculiar changes in the skin that it represents. In its strict sense, these are the only features of the process that it connotes, and, furthermore, we believe that the qualifying term, circumscribed, serves at once to remove attention from any group of constitutional changes that have come to be associated with it. We therefore favor the retention of the term, circumscribed myxedema, as apt, descriptive and historically correct.

SUMMARY AND CONCLUSIONS

1. A case of circumscribed myxedematous infiltration of the skin is presented, together with a tabular summary of the twenty-two similar cases described in the literature.

2. A tuberose, nodular or papular type with diffuse infiltration of the face and a plaque type involving the pretibial region are recognized.

3. The general symptoms of myxedema may be lacking in the tuberose type. The plaque type is always associated with exophthalmic goiter, although it may appear in an interlude in the exophthalmic goiter with symptoms suggestive of a transient myxedema.

4. The microscopic picture, identical in both types, consists, in essence, of mucous infiltration of the cutis, with the appearance of immature connective tissue cells (star cells).

5. Associated disturbance of other endocrine glands may be present, but the picture is dominated by the thyroid gland.

6. The tuberose type, although it apparently does not respond to any medication, may respond to the administration of thyroid, while, so far as we have been able to discover, the plaque type does not.

7. The plaque type may involute spontaneously.

NOTE.—Since our manuscript was submitted for publication, we have observed two cases similar to the one reported. The second case occurred in a Negress, aged 35, with typical exophthalmic goiter. The basal metabolic rate was plus 21. The thyroid gland was not removed. The third case occurred in a white man, aged 49, with a preoperative basal metabolic rate of plus 53. The pretibial plaques increased in size after thyroidectomy. In both cases there was evidence of ankle stasis. Dr. Charles H. Frazier, of the Thyroid Clinic of the University Hospital, permitted us to report the third of these cases, and he gave us the basal metabolic readings. Dr. Fred D. Weidman performed special stains and aided in the interpretation of the histologic picture in the first case.

In June, 1931, the lesions in our original case had almost completely disappeared.

KERATOMA PLANTARE SULCATUM (CASTELLANI) *

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A peculiar condition of the soles and heels, first described by Castellani [1] who named it keratoma plantare sulcatum, is met with in tropical and subtropical climates.[2]

Briefly, the following symptoms may be noticed: There is a marked thickening of the horny layer of the soles, which is most pronounced on the parts in contact with the earth during walking. Here the horny layer contains numerous holes of different sizes and depths, while in the well developed stage of the condition, many fissures, often of an arcuate shape and never extending deeper than to the inner side of the stratum corneum, are also present. Because of the dirt that accumulates in the holes and fissures, they stand out sharply against the yellowish-brown background.

The condition is seen in its most typical form during the rainy seasons. The pitting and fissuring disappear in the dry seasons, and only a much thickened horny layer remains, which is first more or less spongy and soft and later becomes a hard horny substance. In the dry seasons the patients sometimes complain of burning of the feet and pain after much walking, but in many instances all subjective symptoms are lacking.

Castellani and Chalmers mentioned that they ordinarily observed keratoma plantare sulcatum in barefooted natives, and had noticed it in only one European of the better class. In Dutch Guiana I encountered the disease only in the colored races; all the patients belonged to the poorer classes and did not wear shoes.

The condition appears early in life. Most of the patients could not remember when they first became aware of changes in the skin of the soles. In their language, the taki-taki, they call the disease watra-njang (water-eaten), thus recognizing the influence of water in the different stages of the condition. They sharply distinguish it from yaws. I never observed hard, horny plugs, suggesting clavi, unless the condition was complicated by another disease. The palms were never involved. There was normal or slightly increased production of sweat; an oozing or weeping condition due to holes and fissures discharging exudate was never seen. I noticed the disease only in men. A definite hereditary disposition could not be ascertained.

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* Submitted for publication, Jan. 19, 1931.

1. Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, London, Baillière, Tindall and Cox, 1919, p. 2259.

2. Castellani, A.: Notes on Tropical Diseases Met With in the Balcanic and Adriatic Zones (Balcanic Zone), J. Trop. Med. **20**:219 (Oct. 1) 1917.

HISTOPATHOLOGY

After fixation, the preparations showed a considerable degree of hardness because of the thickened, horny layer. Thus it proved difficult to obtain suitable sections, and only thick ones could be studied.

The corium showed small perivascular infiltrates extending to the papillary layer and consisting mainly of lymphocytes. Moderate acanthosis and a slight degree of spongiosis were noticed in the rete malpighii. In one case considerable intracellular edema was present.

The granular layer generally consisted of from six to seven layers of cells, giving rise to a well developed stratum lucidum.

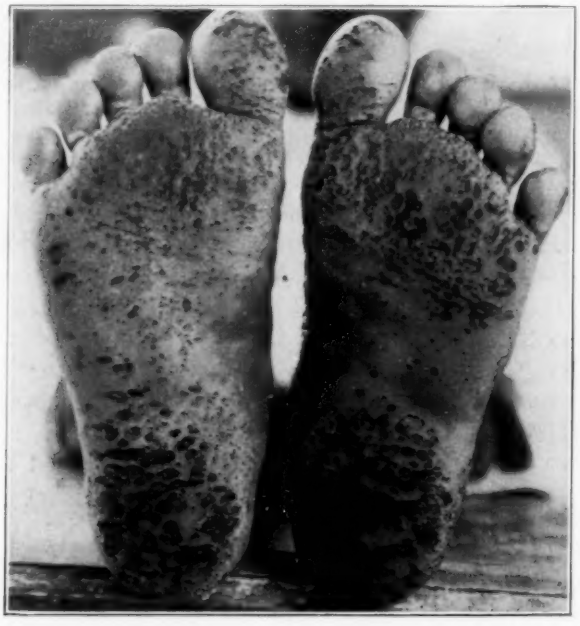

Fig. 1.—Keratoma plantare sulcatum in the fully developed stage.

The stratum corneum was greatly thickened and did not possess nuclei. In some places it showed irregular pits, corresponding to the superficial holes and sulci already mentioned.

ETIOLOGY

According to Castellani, the condition is of unknown etiology, though yaws may play a part in some cases.

Hermans [3] and others often noticed improvement after the administration of arsphenamine. Hermans, however, spoke of the condition

3. Hermans, E. H.: Framboesia Tropica, Amsterdam, H. J. Paris, 1928, p. 85.

as a very painful one, which is not a common observation. Perhaps there were cases of tertiary frambesia among his patients.

Some authors consider the condition among the manifestations of tertiary yaws. Table 15 in the handbook of Plehn and Mense [4] shows the picture of a disease of the sole which Baermann [5] considered to be tertiary yaws. In my opinion this was a case of keratoma plantare sulcatum together with alterations in the skin due to yaws. One must not mistake keratoma plantare sulcatum for the disease of the palms and soles first described by Jeanselme and later by Castellani. In this condition hard papules are present, embedded in the epidermis as horny

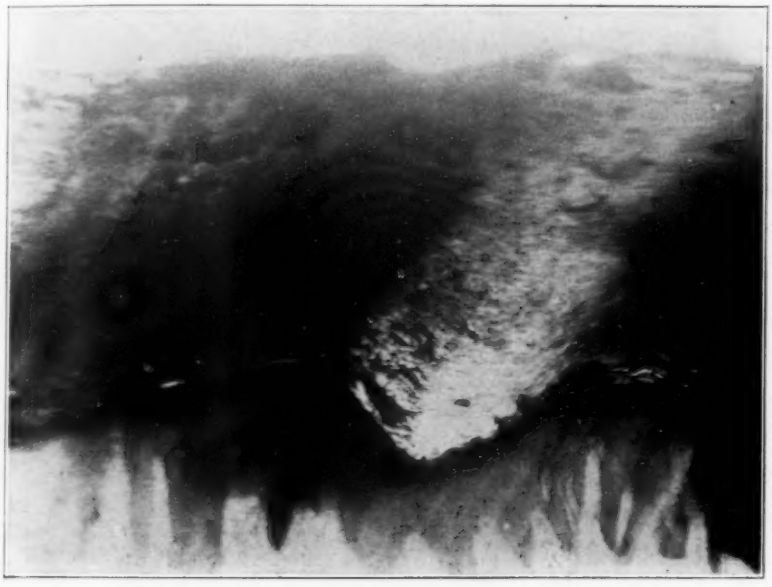

Fig. 2.—Histologic picture of keratoma plantare sulcatum (a good photomicrograph could not be obtained). Note the moderate acanthosis and the considerable hyperkeratosis.

plugs and pearls, leaving deep depressions after their disappearance. Salanoue-Ipin [6] considered this a symptom of secondary yaws.

4. Plehn, A., and Mense, K., Jr.: Die tropischen Hautkrankheiten, in Mense, C.: Handbuch der Tropenkrankheiten, Leipzig, Johann Ambrosius Barth, 1924, part 2, p. 629.

5. Baermann, G.: Die spezifischen Veränderungen der Haut der Hände und Füsse bei Frambösie mit einigen allgemeinen Bemerkungen zur Frambösie und ihren Späterscheinungen, Beihefte z. Arch. f. Schiffs- u. Tropen-Hyg., 1911, vol. 15.

6. Salanoue-Ipin: Pian, in Grall, C., and Clarac, A.: Traité de pathologie exotique, Paris, J. B. Baillière et fils, 1919, p. 206.

In a recent paper, Acton and McGuire [7] proposed a different etiology for keratoma plantare sulcatum. They observed a disease of the soles in Bengal which they called keratolysis plantare sulcatum instead of keratoma plantare sulcatum (Castellani). In their cases hyperkeratosis as well as plugging were absent, but there was definite lysis of the horny layer. Occasionally lesions were present on the palms. Aided by a special staining method, they found an *Actinomyces*-like fungus in eight

Fig. 3.—Keratoma plantare sulcatum associated with secondary yaws.

cases, while the fungus could be cultivated in two of the cases. They reported, however, that the same fungus was found in cases of intertrigo, paronychium and hyperkeratosis of the soles and palms. Though the condition they described showed seasonal incidence like keratoma plantare sulcatum, the absence of hyperkeratosis and the involvement of the palms in some patients are not common in the latter disease.

7. Acton. H. W., and McGuire, C.: Keratolysis Plantare Sulcatum, a Lesion Due to an Actinomycotic Fungus, Indian M. Gaz. **65**:61 (Feb.) 1930; cited from Trop. Dis. Bull. **27**:523 (July) 1930.

Fig. 4.—Typical granulomatous eruption in early secondary yaws.

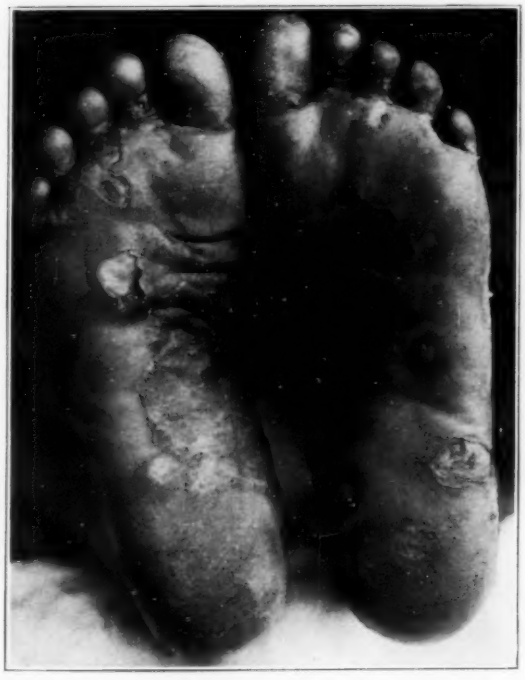

Fig. 5.—Later stage of untreated secondary yaws. Note the typical squamous collars of the lesions.

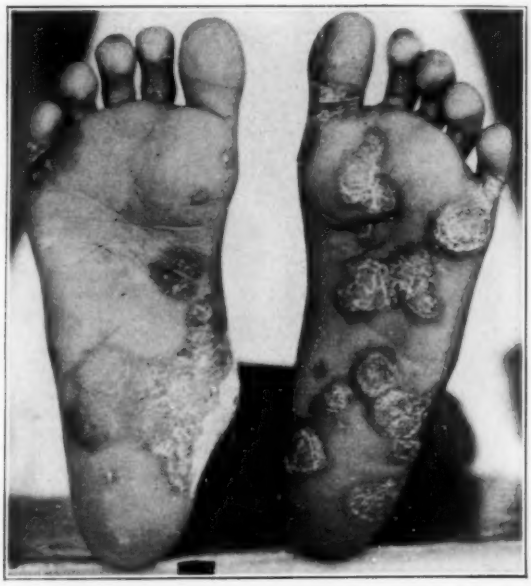

Fig. 6—Late papulosquamous secondary yaws, occurring in a Bush Negro girl, aged 12 years, who had suffered from a general eruption of yaws two years before, and in whom signs of syphilis were absent.

Fig. 7.—A high degree of dermatophiliasis.

My cases, observed in Dutch Guiana, did not show any evidence of a fungus infection. Many fungi could easily be isolated from the surface of the soles, but I could only consider them common saprophytes, without any etiologic bearing on the disease. Moreover, I think that one must be careful not to overemphasize the finding of superficially located fungi in tropical dermatoses. I could not attribute the condition to yaws. Against the theory that yaws plays an important rôle in the

Fig. 8.—Arsenical keratosis after neoarsphenamine intoxication.

origin of keratoma plantare sulcatum are the following facts: (1) the regular influence of the seasons, which never cause as many alterations of the skin in conditions due to syphilis or to frambesia; (2) absence of involvement of the palms; (3) negative serum reactions; (4) lack of influence of antisyphilitic treatment (arsenic, bismuth, mercury); (5) the beginning of the condition in early childhood, without a previous history of yaws, and (6) the observations in the following case.

A British-Indian boy, aged 12, who suffered from generalized granulomatous secondary yaws, showed on one of his soles typical

lesions of the secondary stage together with keratoma plantare sulcatum. The boy and his parents said that the last-named condition had existed for years before yaws developed. Further, they stated that the eruption of secondary yaws on the soles had displaced some parts of the earlier disease. During the painful stage the patient had walked on his heels, thus preventing the traumatic formation of holes and fissures in the anterior part of the sole.

On account of the cases that I observed, I can agree with Chalmers and Kamar,[8] who considered the disease as distinct from the punctate keratodermias, which simulate a clinical entity because of the punctate lesions, but cannot be considered identical, according to Sweitzer[9] and others.

Keratoma plantare sulcatum shows such characteristic features that not many difficulties will arise in the recognition of the condition. However, photographs of some diseases of the soles occasionally seen in Dutch Guiana are shown.

COMMENT

Clinical and microscopic anatomic studies lead to the conclusion that keratoma plantare sulcatum (Castellani) should as yet be considered a condition of unknown etiology. Certainly it cannot be regarded as one of the alterations of the soles occurring in yaws. Assuming that the cases described by Acton and McGuire were cases of keratoma plantare sulcatum, I cannot share their opinion that it is possibly a fungus infection.

It would be simplest to consider the disease as a primary hyperkeratosis. In the dry seasons there is a rather diffuse thickening of the horny layer, whereas during the rainy seasons the horny masses become soaked and trauma is likely to punch out the most softened parts of the soles. Because of the long distance the sweat has to course in the horny layer, the most thoroughly soaked parts will be found immediately adjacent to the sweat ducts, and here the first holes will appear.

If one follows the classification of Chalmers and Atiyah,[10] the disease should be reckoned among the nonfollicular localized forms of the primary hyperkeratoses, which they divided into (*a*) keratodermias, (*b*) acanthokeratodermias and (*c*) angiokeratomas. Keratoma plantare sulcatum then belongs to the keratodermias, of which Chalmers and

8. Chalmers, A. J., and Kamar, A.: Keratodermia Punctata, J. Trop. Med. **20**:121 (June 1) 1917; Further Notes on Keratodermia Punctata, ibid. **20**:218 (Oct. 1) 1917.

9. Sweitzer, S. E.: Keratodermia Punctatum, Arch. Dermat. & Syph. **8**:687 (Nov.) 1923.

10. Chalmers, A. J., and Atiyah, S.: Acanthokeratodermia praecornufaciens, J. Trop. Med. **20**:23 (Feb. 1) 1917; 37 (Feb. 15) 1917.

Atiyah gave the following definition: "These are localized non-follicular primary hyperkeratoses without marked acanthosis and without markedly dilated papillary vessels." Although acanthosis can be seen in the sections, it is present only in a moderate degree.

Following the classification of Darier,[11] the condition might be placed among the "kératodermies (kératoses palmaires et plantaires)" in the group of the regional keratoses. Perhaps it would be more to the point, therefore, to call the disease keratodermia plantaris sulcata (Castellani).

Because of the difficulty of taking histories in my cases, a definite hereditary factor could not be determined.

11. Darier, J.: Précis de dermatologie, Paris, Masson et Cie, 1928, p. 247.

BILATERAL HERPES ZOSTER FOLLOWING ACUTE ARSENIC POISONING

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A résumé and photographs of this case are presented because of its unusual character and the circumstances that preceded it.

REPORT OF A CASE

History.—Mrs. E. D., a white woman aged 73, was admitted to the Pittsburgh Hospital, service of Dr. C. J. Devlin, on Sept. 14, 1930, complaining of pain and stiffness in all of the extremities, particularly in the legs.

The history showed that on Sept. 5, 1930, she had eaten some biscuits made with loose flour that had been purchased at a grocery near her home. About one-half hour after eating, she became violently nauseated and vomited profusely, and the other members of her family were likewise affected. All were somewhat ill during the night, and the following morning had nausea and diarrhea, which they attributed to food poisoning. The next evening noodles were made with the same flour and again all members of the family were ill in exactly the same manner. All of them recovered promptly except Mrs. D. and one son, aged 20. In these two pain, stiffness, weakness and some swelling developed, particularly in the legs. As this condition continued, they consulted Dr. Devlin, who admitted them to the hospital for observation. After the second illness they had decided that the flour was at fault, because a pet dog became violently ill after eating some of the noodles, and some of the flour was saved for examination. The Pennsylvania Department of Agriculture also obtained a sample of the flour from the store. Examination showed that it contained arsenic. A quantitative analysis was not made, but small quantities of the flour were fatal to white rats.

Examination.—On admission examination showed a healthy looking woman lying comfortably in bed. There were no gross evidences of any pathologic condition. General examination gave normal results, and the general history was entirely unimportant. There was a slight edema of the legs and the pitting on pressure was slight. There was a noticeable weakness of the hands and a laxness of the ankles, which suggested wrist and ankle drop, but this symptom was not marked enough to disturb the patient. The blood count was not indicative of any disease, and urinalysis showed only a faint trace of albumin and a few granular casts. The patient was placed on a diet of soft foods and given treatment to increase elimination. She gradually improved, and for six days she believed that she was growing stronger each day. On the sixth day in the hospital she complained of headache and pain in the back and legs; this pain was quieted with a mild sedative. On the seventh day there was some evidence of rash, and the dermatologic department was called in consultation.

The patient was seen on the eighth day of hospitalization, which was the eighteenth day after eating the flour. In the lumbar region on the right side a well developed herpes zoster was observed. The groups of vesicles were not

* Submitted for publication, Dec. 12, 1930.

* From the Department of Dermatology, University of Pittsburgh.

Fig. 1.—Distribution of vesicles on the neck of a patient with herpes zoster due to acute poisoning with arsenic.

Fig. 2.—Extensive distribution of discrete vesicles on the right side of the back of a patient with herpes zoster.

large, but they were numerous and extended on the right side from the spine to the midline of the abdomen. Numerous discrete vesicles were scattered among the groups; they were tense, and practically all of them were infected. On the left side of the neck and extending down over the back, the arm and the chest, there was another severe but less extensive herpes zoster. The groups of vesicles on the neck were numerous, but in the other three areas they were only scattered. There was no extension of the process either to the face or the scalp. Pain was slight in both areas, and mild antiseptic applications were prescribed.

Course.—In about one week the eruption was practically healed, and only a few crusts were present. The temperature never rose above 99.2 F., and the pulse rate never rose above 96 per minute. During this time the other symptoms improved, and the patient was discharged as improved on Sept. 30, 1930.

The son showed wrist and foot drop, but a rash did not develop. His convalescence was more prolonged.

7026 Jenkins Arcade.

FUMIGATION AS AN AID IN THE CONTROL OF SUPERFICIAL FUNGUS INFECTIONS*

SAMUEL AYRES, JR., M.D.

NELSON PAUL ANDERSON, M.D.

AND

ESTHER M. YOUNGBLOOD

LOS ANGELES

No originality is claimed for the idea of fumigation, as this procedure has doubtless been used on numerous occasions to achieve sterilization of material contaminated by fungi, just as it has been used in connection with such infectious diseases as smallpox, scarlet fever, etc. But, curiously enough, it has rarely been mentioned in the voluminous literature that has been accumulating during the past few years on infections of the skin due to fungi, and judging by conversations with a number of colleagues, it seems to be a phase of the treatment that has been largely neglected.

The amazing spread of epidermophytosis or ringworm of the foot has forced this condition on the attention of the entire population, until at present it is dividing honors with acute respiratory infections, such as common colds, sinusitis, etc., for popular attention. The problem is greater than a matter of individual treatment; the disease is epidemic, and although usually not a menace to life, it may lead to considerable discomfort, economic disability and, through secondary streptococcic infections, occasionally even to a fatal termination. Many patients acquire the infection by walking barefoot on infected floors of gymnasiums, swimming pools, athletic and country clubs. School gymnasiums are also a common source of infection. The problem is a matter of public health; not only must the individual be cured, but the source of infection must be eradicated.

The remedies employed in the treatment for epidermophytosis are almost as numerous and varied as the authors who have written on the subject, but in our opinion little improvement has been made over the application of Whitfield's original ointment, one formula of which is as follows: salicylic acid, 2 Gm.; benzoic acid, 4 Gm., and benzoinated lard, 30 Gm.

Almost without exception, patients with the condition who have been treated elsewhere have not been advised regarding sterilization of their shoes, stockings or floor. It has been shown that spores of *Epidermophy-*

* Submitted for publication, Jan. 3, 1931.

ton[1] may remain viable on the ground as long as a year or more. It is difficult therefore to see how a permanent cure can be expected in this disease if the patient is merely given an ointment and not instructed in regard to preventing recurrences. It is a comparatively simple matter to relieve the patient in an attack by prescribing any one of a number of suitable remedies, but without adequate sterilization of shoes, stockings, bath mats and bedroom and bathroom floors, subsequent attacks,

Fig. 1.—Photograph of test tubes containing cultures of Microsporon lanosum. No growth appeared in tubes 1 and 3, in which the material had been exposed to fumes from a formaldehyde candle, but it did appear in tubes 2 and 4, in which transplantation of the same, unfumigated material was made.

as well as a spreading of the disease to other members of the family, are almost inevitable.

Even though socks can be boiled for a prolonged period, shoes and floors cannot be subjected to this treatment, and discarding the shoes (an expensive procedure) still leaves the floors to spread the infection.

1. Farley, D. L.: Viability of Ringworm in Dry Cutaneous Material, Arch. Dermat. & Syph. **3**:759 (June) 1921.

Antiseptic solutions and disinfectants are difficult to apply to carpeted floors. Some country clubs have adopted the use of paper slippers ("sani-treads") for protection against the bare floors.

Fumigation with a formaldehyde candle is a simple and effective method of sterilizing all of the materials with which the infection has come in contact. The following experiment was undertaken to determine the effectiveness of this procedure.

METHOD

The susceptibility of three of the more common types of pathogenic fungi to the fumes of formaldehyde was studied: *Epidermophyton* (Kaufman-Wolff), *Monilia albicans* and *Microsporon lanosum*. In each instance, fresh material from

Fig. 2.—Cultures of epidermophyton from the same source. Growth took place in the control tubes, 2 and 4, within from four to ten days, but the tubes containing fumigated material, 1 and 3, remained sterile for an indefinite period (forty-three days at the time of this report).

active lesions as well as dried material from old cultures was used. The material to be sterilized was placed on the floor of a room approximately 9 by 12 feet, and corresponding material was planted on fresh tubes of Sabouraud's medium as controls. Before placing the formaldehyde candle in the room, hot water was allowed to run into a basin for ten minutes to increase the humidity of the room, since the fumes penetrate more rapidly in the presence of moisture. The same result could have been attained by having a basin of steaming hot water in the room before and during the fumigation. The windows and doors were closed and the cracks stuffed with paper. The candle was then lighted, and the room was kept closed for four hours. At the end of the period the samples of material were planted on fresh tubes of Sabouraud's medium, and they and the controls

were allowed to remain in a dark closet at room temperature. Growth took place in each of the control tubes within from four to ten days, but all of the tubes containing fumigated material have remained sterile up to the time of writing this paper (forty-three days).

The accompanying table illustrates the results of this experiment.

Susceptibility of Three Types of Fungi to Fumes of Formaldehyde

Organism	Source of Material	After Exposure to Formaldehyde Fumes	Controls
Epidermophyton...	Scales from infected foot	No growth 43 days	Pure culture in 4 days
	11 months old culture	No growth 43 days	Pure culture in 4 days
Microsporon lanosum	Infected scalp hairs	No growth 43 days	Pure culture in 7 days
	11 months old culture	No growth 43 days	Pure culture in 7 days
Monilia albicans....	Scales from mouth lesions	No growth 43 days	Pure culture in 10 days
	9 months old culture	No growth 43 days	Pure culture in 6 days

COMMENT

In the practical application of this procedure, patients should be instructed to place all of their shoes, slippers, athletic shoes, socks, stockings, bath mats and any other material coming in contact with their feet in the bedroom or bathroom and to fumigate both rooms. It is preferable to fumigate once about one week after the patient has begun the use of an antiparasitic remedy locally, and once more after he is clinically and microscopically free from the disease. In cases of active infections of the hands or crotch, the gloves, golf clubs, underwear, athletic supporters, etc., should be fumigated, and in cases of ringworm of the scalp, all hats, combs, brushes, etc.

A remedy, especially local remedies that are excessively irritating, should not be employed for an indefinite time. The type of medication commonly employed for fungus diseases is necessarily irritating, and if used injudiciously an eczematous condition may be substituted for the original infection. Microscopic examination of scales macerated in 40 per cent potassium hydroxide should be made prior to the institution of treatment and at intervals until organisms can no longer be found. Intermittent treatment for about two weeks after the skin is microscopically and clinically well, combined with fumigation, as has been described, and careful attention to infected toe-nails, which, Williams [2] pointed out, may act as a focus of reinfection, should give a considerably higher percentage of permanent cures than is commonly obtained.

SUMMARY

An experiment is described in which infected material from active lesions as well as dried material from old cultures of three common

2. Williams, C. M.: Tinea of the Nails as a Source of Reinfection of Tinea of the Feet, Arch. Dermat. & Syph. **18**:730 (Nov.) 1928.

pathogenic fungi was exposed for four hours to the fumes from a formaldehyde candle in a closed room. Fresh tubes of Sabouraud's medium inoculated with this fumigated material remained sterile indefinitely (forty-three days). In control tubes inoculated at the same time with identical material that had not been fumigated pure cultures of the respective organisms developed within from four to ten days.

In view of this experiment, it is believed that more permanent results in the treatment for epidermophytosis and other fungus infections will be obtained if patients are instructed to place all shoes, socks, slippers and other infected articles of clothing in the bedroom or bathroom and to fumigate both rooms.

Periodic fumigation of gymnasiums and locker and shower rooms would probably be effective in curbing the epidemic proportions of this disease.

HODGKIN'S DISEASE

SURFACE LYMPHOGRANULOMATOSIS CONFINED TO THE ORAL AND THE PENILE MUCOSA; REPORT OF A CASE *

HERMAN SHARLIT, M.D.
NEW YORK

The cutaneous manifestations of Hodgkin's disease have been divided into two groups: (1) infiltrative changes characteristic of the disease, which show (though not always) the histologic picture of cellular infiltration described by Sternberg and Reed and (2) nonspecific, toxic eruptions. Among the former group, lesions of the mucous membrane have been of uncommon occurrence and when they occurred it was only in association with cutaneous lesions. The case herein reported is apparently unique in that the mucous membrane alone was involved, and that the lesions were granulomas.

REPORT OF CASE

History.—J. J. S., a white man, aged 52, who was first seen in September, 1926, and whose family and personal histories were irrelevant, stated that he had had swollen glands since late in 1924, and that he had never had a cutaneous eruption or sore mouth until one month before his first visit to me. He was admitted to the Roosevelt Hospital in New York City in June, 1926, where he was given deep roentgen therapy for intra-abdominal and intrathoracic adenopathy. At this time examination of an excised superficial lymph node led to the diagnosis of Hodgkin's disease. The patient was discharged from the hospital as improved several weeks before he came to me.

Examination.—Examination showed a patchy exfoliation of the membranous lining of the prepuce, glans penis, tongue, lips and buccal mucosa. A larygnoscopic examination revealed no involvement of the mucous membrane beyond that visible on inspection of the oral cavity. There was no striking enlargement of the superficial chains of lymph nodes, except those draining the penis and the mouth. The inguinal nodes were greatly enlarged bilaterally, as were the submental and the submaxillary nodes. At the angles of the jaws there were single nodes the size of pigeon's eggs. The patient could not state with certainty whether the regional adenopathy preceded or followed the involvement of the mucous membrane, and he could not state definitely that there had been a previous formation of bullae over the denuded areas of the mouth and the penis. Examination revealed no evidence of such evolution of the lesions, and subsequent observation confirmed the opinion that denudation was preceded by a slow lifting of the epidermal layers, without formation of vesicles, leaving red, raw, oozing surfaces. Elsewhere on the body, the skin showed no abnormality beyond a striking pallor due to marked secondary anemia.

* Submitted for publication, Dec. 24, 1930.

The patient was presented at the Section of Dermatology and Syphilology, New York Academy of Medicine, in December, 1926, and the discussion of the case brought out the possibility that the eruption was caused by a drug, particularly phenolphthalein. Subsequent bimonthly observation of the patient permitted testing of the hypothesis that the eruption was due to drugs. Questioning had failed to reveal that the patient had previously used a medicine known to contain phenol-

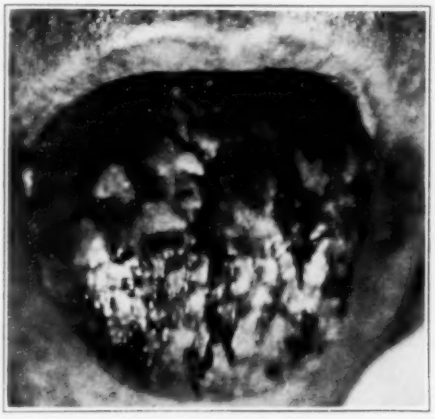


Fig. 1.—Appearance of the tongue in the case reported.

Fig. 2.—The glans penis, showing the patchy exfoliation of the lining membrane.

phthalein. In the course of the next few months phenolphthalein, antipyrine, salicylate and acetphenetidin were administered with the result that if any change occurred in the lesions it was in the nature of an improvement.

Readmission.—In April, 1927, the patient's general condition had grown alarmingly worse; fluid had reaccumulated in the chest and the abdomen, and respiration was labored. He was readmitted to the Roosevelt Hospital in May, 1927, and

one deep roentgen treatment was given to the chest in addition to thoracic and abdominal paracentesis. I saw him again in October; he was greatly emaciated and feeble, with hypostatic congestion in the lungs, but the lesions in the mouth had entirely disappeared. The balanitis still remained unchanged. The nodes about the jaw had disappeared; those in the groin were unchanged. The patient stated that the nodes about the jaws had shriveled about two weeks after the roentgen treatment of the chest and that the lesions of the mouth had healed soon after that. The patient died on November 12.

Laboratory Observations.—Blood counts made at intervals during the year in which the patient was under observation disclosed only the picture of a profound secondary anemia and a tendency toward relative lymphocytosis. The urine always showed traces of albumin; it never showed sugar, but occasionally there was acetone. Three examinations of the stool for mucus or blood gave negative results.

Histologic Observations.—Histologic examination of the lesions on the prepuce showed that the epidermis was edematous and lifted away from the corium by a serosanguineous exudate. The corium, particularly the subepithelial area, was densely infiltrated by cellular elements. They consisted chiefly of mononuclear leukocytes and epithelioid and endothelial cells. Included in these masses were fibroblastic and reticular cells with scattered eosinophils, the latter appearing distinctly related to the presence of extravasated blood. No cells characteristic of the type described by Sternberg and Reed were seen. The blood and lymph channels were markedly distended.

This picture permits of the diagnosis of granuloma. On examination of a section of the tissue, two histopathologists concurred with this opinion.

COMMENT

Granulomatous changes along the lining of the gastro-intestinal tract and in the oral cavity have previously been observed in Hodgkin's disease. In this case the unique observation is the limitation of the changes in the mucous membrane to the visible portions of mucosa that are ordinarily seen by the dermatologist. Certain of the clinical features in this case are of more than passing interest: (1) the enlargement of the superficial lymph nodes only in the chains draining the affected parts, and (2) the complete clearing up of the lesion in the mouth subsequent to a shrinkage in the size of the regional lymph node consequent on roentgen therapy (deep therapy administered to the chest apparently brought the jaws into the field of exposure). Unfortunately, the patient could not state with certainty whether the adenopathy preceded or followed the eruption of the membrane; however, the sequence of events in their disappearance is clear and definite. A changed state in the regional lymph nodes may cause a disappearance of a granuloma of Hodgkin's disease, and such a change may be successfully induced by filtered roentgen therapy.

853 Seventh Avenue.

Correspondence

KERATODERMA BLENNORRHAGICUM

To the Editor:—I enclose photographs taken in two cases of keratoderma blennorrhagicum, which may be of interest as a matter of record.

It would be needless for me to make any comments on the subject, as I do not know of anything new not published in the several able articles recently published in the ARCHIVES.

The patient in case 1 died a few months ago after undergoing a severe illness. All the large joints and the articulations of the neck and jaw were so fixed that he was unable to move, bend his head or open his mouth. At one time

Fig. 1 (case 1).—Lesions on the hand.

there was a complete exfoliation of the skin of both hands as far as the wrists. He suffered greatly with arthritis. This man had been a resident of Honolulu since birth. The test for gonorrhea was positive.

The patient in case 2 was a Filipino laborer recently imported from the Philippines to work on a sugar plantation. Those in medical attendance were unable to make a diagnosis until I returned home on March 25, 1931. Unfortunately, the photographer failed to take pictures showing the involvement of the joints, as was done in the first case, but they were similar. The test for gonorrhea was positive.

The patient in case 3, a young Hawaiian woman, was seen by me about three years ago. I have been unable to trace her since she left the hospital, but she is living somewhere in Honolulu.

Fig. 2 (case 1).—Appearance of the legs.

Fig. 3 (case 1).—Involvement of the joints of the hand.

I believe that there have been reported but three or four cases in women; therefore, this case may be of interest. Of the ninety or more cases now reported, only three were from Hawaii. Two patients had been residents in Honolulu since birth and the third had recently arrived.

Fig. 4 (case 2).—Lesions on the feet.

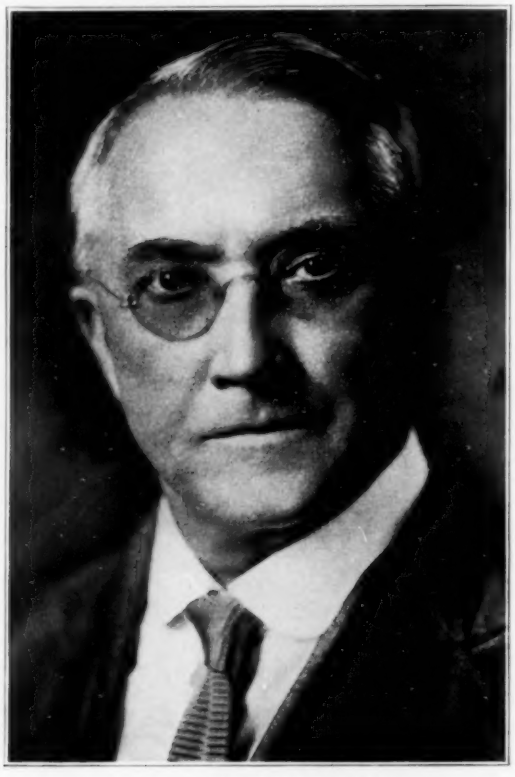
I have made no attempt to describe the lesions, as they are typical and have been well described by those more capable than I.

JAMES T. WAYSON, M.D., HONOLULU, T.H.,
Assistant Administrator, Territorial Board of Health, Hawaii;
Medical Director, Bureau of Leprosy and General Health Officer.

Obituary

J. B. SHELMIRE, M.D.
1858-1931

Dr. J. B. Shelmire, emeritus professor of dermatology at Baylor Medical School, died on July 9 at Dallas, Texas. He was in active practice and enjoyed perfect health until the last days of his life. On July 5 he was stricken with acute appendicitis; an operation performed a few hours later revealed a gangrenous appendix.



J. B. SHELMIRE, M.D.
1858-1931

Dr. Shelmire was born in Port Hudson, La., on Feb. 13, 1858. He received a Bachelor of Arts degree from Centenary College in 1878, and his medical degree from Tulane University in 1883. For the next ten years he practiced general medicine in a small community in Louisiana.

In 1894, he went to New York and studied dermatology. At the completion of this training, he moved to Dallas, Texas, and began the

practice of dermatology and urology. His real interest, however, was in dermatology, and it was not long until he confined his practice entirely to that branch of medicine.

He was the pioneer dermatologist of the Southwest and one of the first specialists in any branch of medicine in Texas. It was pioneering of the real sort, requiring patience, integrity, industry and courage, but he was successful and in a few years had securely established himself. Indeed, for years he was the only disciple of dermatology in an extensive territory; despite this isolation he kept wonderfully abreast of the advances in medicine and steadily built up a solid edifice of respect for himself and for the specialty he represented.

From 1905 to 1915, he was professor of dermatology in the medical department of Southwestern University. When that school closed in 1915, he accepted the chair of dermatology in Baylor Medical School and taught there until his retirement from active teaching in 1927.

He was an active member of his county and state medical societies, of the Southern Medical Association and of the American Medical Association. He was also a member of the American Dermatological Association and a collaborating editor of the *Acta dermato-venereologica*. He was one of the first chairman of the Section of Dermatology and Syphilology of the Southern Medical Association.

Dr. Shelmire published many articles in the journals of his section of the country but was an infrequent contributor to periodicals of national scope. He was the first to suggest the use of the ethyl chloride spray in larva migrans.

He was sincerity itself; direct in speech, candid but never spiteful. There was always an air of good humor about him that revealed a tolerant and kindly spirit.

Dr. Shelmire is survived by his wife, three daughters and a son, Bedford, who was associated with him in practice.

Abstracts from Current Literature

THE TREATMENT OF CARDIOVASCULAR SYPHILIS WITH ESPECIAL REFERENCE TO AORTIC REGURGITATION WITH CONGESTIVE HEART FAILURE. G. HERRMANN and C. JAMISON, Am. J. Syph. **15**:1 (Jan.) 1931.

From the point of view of the efficacy of the various therapeutic regimens, the authors analyzed the treatment in 100 cases of syphilitic aortic regurgitation which they were able to follow up closely. Negroes constituted 70 per cent of the patients, while Caucasians made up 30 per cent. Sixty per cent of the patients died.

The average interval between the date of the appearance of the chancre and the onset of cardiac symptoms was nineteen years and seven months. The average length of time between the development of the chancre and death was twenty-five years.

The first therapy in decompensated cases consists of circulatory supportive measures rather than antisyphilitic drugs. Digitalization by the slow method of small doses was apparently the safest and most efficient cardiovascular therapy, especially when combined with the administration of theophylline preparations.

The authors present a number of tables from which no definite conclusions can be drawn regarding the value of antisyphilitic therapy for decompensated syphilitic aortic regurgitation. In general, following the reestablishment of the circulatory equilibrium, the milder forms of treatment with iodides, mercury and bismuth had most in their favor. The number of patients treated with neoarsphenamine after preparatory treatment with iodides, mercury and bismuth was small, but they seemed to do well. The authors warn against the intravenous use of arsenicals until after from two to three months' treatment with mercury, bismuth or iodides.

The application of the therapeutic measures outlined seemed to add to the total span of life of patients with decompensated syphilitic aortic regurgitation, and, in addition, the patient was made much more comfortable.

The difficulty with a report such as this is that accurate estimation or evaluation of treatment, while most desirable, is impossible.

THE TREATMENT OF SYPHILIS IN TUBERCULOUS PATIENTS. MAURICE SULLIVAN, Am. J. Syph. **15**:37 (Jan.) 1931.

This study was made from the records of 1,000 patients with tuberculosis admitted to the general medical wards and the Dibert Memorial, Charity Hospital, New Orleans. Most of the patients had pulmonary tuberculosis . In this series, the incidence of syphilis was 11.6 per cent. The death rate among patients with tuberculosis complicated by syphilis who were given antisyphilitic treatment was 14 per cent, as contrasted with a death rate of 40.8 per cent when the patients were not treated.

The author does not offer anything new, but reiterates the commonly accepted therapeutic principles in the treatment for tuberculosis complicated by syphilis.

SYPHILITIC JUXTA-ARTICULAR NODES. LOUIS A. BRUNSTING, Am. J. Syph. **15**:42 (Jan.) 1931.

The author reports three cases of juxta-articular nodes occurring in three men who had never been in the tropics and who showed definite evidence of syphilis. The Wassermann reaction was positive in all three cases; in two, there was definite evidence of visceral syphilis. In two cases the lesions were multiple and located over the palms, fingers and elbows. In the third case, the lesion was solitary and located over the left elbow. Detailed histopathologic changes are

reported in each case. In only one case were the microscopic observations of sufficient degree to warrant a diagnosis of syphilis. In the other cases, the histopathologic changes were chronic, nonsyphilitic and inflammatory. The response to treatment of the patient who did not show evidence of syphilis other than a positive Wassermann reaction was complete; in another, the solitary lesion was excised, while in the third, sufficient time had not elapsed to permit an evaluation of the response to treatment.

This report serves to strengthen the hypothesis that juxta-articular nodes can be the products of syphilis.

CONCERNING THE CURATIVE VALUES OF CERTAIN BISMUTH COMPOUNDS. S. S. GREENBAUM and A. M. RULE, Am. J. Syph. **15**:59 (Jan.) 1931.

This study of the curative values of various bismuth compounds was made on rabbits by the tissue transfer method. There was an extreme variation in the spirocheticidal properties of the various compounds studied which did not depend on the amount of bismuth in the compound or on the total amount injected. However, experimental results are not always safest to follow, since brilliant effects following the treatment with bismuth for syphilis in rabbits does not necessarily mean that the same will follow the treatment for syphilis in human beings.

The authors warn against the use of the same dose for all bismuth compounds, and urge that only the few preparations that have been extensively studied from a clinical standpoint be used in the treatment for syphilis and that new preparations be carefully investigated before being utilized. In the light of present knowledge, if a compound is used that is less rich in bismuth metal, an increased number of injections is usually indicated.

TRANSMISSION OF SYPHILIS BY BLOOD TRANSFUSION. S. H. POLAYES and MAX LEDERER, Am. J. Syph. **15**:72 (Jan.) 1931.

The authors report the case of an infant in whom syphilis developed following a transfusion of blood. Apparently the syphilis was acquired from the donor. Ten cases of this nature reported in the literature are reviewed, and pertinent facts regarding the suitability of the blood of donors are discussed.

M. J. REUTER, Milwaukee.

ARTIFICIAL SENSITIZATION OF INFANTS TO POISON IVY. H. W. STRAUS, J. Allergy **2**:137 (March) 1931.

A poison ivy extract applied as a patch test to 41 normal and atopic adults gave a positive test in 75.6 per cent of the cases, while in 119 new-born infants this test was completely negative. After an interval of from two to four weeks, 48 of the infants were retested by the same patch method and a positive reaction was obtained in 35 cases, or 72.9 per cent.

The author concludes from this that the insusceptibility of children under the age of 3 years to poison ivy is due to lack of previous contact, and that newborn infants may be artificially sensitized to poison ivy by skin contact with a potent extract.

"PHYSICAL ALLERGY:" REPORT OF A CASE WITH SUCCESSFUL TREATMENT. H. L. ALEXANDER, J. Allergy **2**:164 (March) 1931.

A woman, aged 53, had suffered from urticaria for twenty-five years, each attack coming on after exertion and overheating. In an attempt to exhaust the mechanism underlying the production of hives, the patient was immersed in warm water. This was followed by an intense urticarial eruption. The bath was gradually made warmer and of longer duration, and the symptoms diminished until finally the patient became tolerant to heat and exercise.

URTICARIA DUE TO GRASS POLLEN. S. J. TAUB and CLEVELAND WHITE, J. Allergy **2**:186 (March) 1931.

Each summer a young woman developed urticaria without mucous membrane lesions, which was unaffected by therapy and which disappeared spontaneously with the onset of cool weather. Skin tests showed that she was sensitive to spring grass pollen, and attacks were controlled by avoidance of exposure.

CARO, Chicago.

PROMOTION OF PHAGOCYTOSIS BY CALCIUM GLUCONATE, SODIUM IODIDE, DEXTROSE AND OTHER SUBSTANCES. RUTH TUNNICLIFF, J. Infect. Dis. **48**:16, 1931.

The leukocytes in the whole blood of rabbits that received intravenous injections of calcium gluconate, calcium chloride, sodium salicylate, sodium iodide, dextrose and neoarsphenamine showed a marked increase in phagocytosis, while physiologic solution of sodium chloride, distilled water, milk, sodium phosphate and mercurochrome in water or in dextrose, also injected intravenously, did not increase phagocytosis. Intravenous and intramuscular injections of calcium gluconate both produced increased phagocytosis, but the increase following the intravenous use commenced twenty-four hours sooner than that from the intramuscular. The increased phagocytic activity induced in a man who received calcium gluconate intravenously, intramuscularly and by mouth returned to normal shortly after the drug was discontinued. In vitro studies with the material used for injection into rabbits gave results similar to those from the in vivo tests.

PRECIPITATION WITH CEREBROSPINAL FLUIDS. A. M. MALLOY, R. L. KAHN and LUCY WESTALL, J. Infect. Dis. **48**:203, 1931.

The authors found that like the Kahn reaction, the colloidal gold and mastic reactions depend on the globulin fraction of the spinal fluid. The albumin fraction gave negative results. The globulin fraction alone gave more sensitive results than the unfractionated spinal fluid. They believe that the precipitin substances in a globulin solution are not the same for the Kahn test as those for the colloidal gold and mastic tests. They base this belief on the fact that the latter two tests can be performed on the supernatant, centrifugated fluid obtained from the globulin solution of the spinal fluid that was used for a previously performed Kahn test. All three tests are little affected by heating the globulin fraction for two hours at 56 C., but when the heating is continued for twenty-four hours a decreased sensitivity follows, particularly in the Kahn test. The colloidal gold and mastic tests are little affected, while the Kahn test is markedly less sensitive when the globulin fraction is heated between temperatures of 56 and 65 C. The sensitivity of the Kahn test is much more decreased than that of the other two tests when heat of 70 C. is used for thirty minutes. The authors feel that these heating experiments also indicate that the Kahn test does not depend on the same conditions that govern the colloidal gold and mastic tests.

CORNBLEET, Chicago.

MYCOSIS FUNGOIDES FOLLOWING LAPAROTOMY. R. OWEN-JONES, Brit. M. J. **1**:537 (March 28) 1931.

The patient was operated on for a perforated duodenal ulcer. There had been no previous cutaneous disease. During the second week an area of cellulitis appeared at the site of the drainage wound in the right loin. This area spread and gradually took on the appearance of an ulcerated granuloma, the microscopic appearance of which corresponded to that of granuloma fungoides. The lesion resisted all treatment. The laparotomy wound was not affected. The patient died after ten months.

CUTANEOUS INFECTION WITH A DIPHTHEROID BACILLUS. J. F. D. SHREWSBURY, Brit. M. J. **1**:538 (March 28) 1931.

A woman, aged 55, developed on the thigh a tender papule, which became pustular, ruptured and finally formed a persistent irregular ulcer about 1½ inches in length. The seropurulent discharge yielded organisms similar to the Klebs-Löffler bacillus. They were found to be similar in every respect except the production of toxin. The lesion was treated surgically.

EPITHELIOMA OF THE PENIS. W. MAXWELL and H. M. MORAN, M. J. Australia **1**:409 (April 4) 1931.

The authors obtained successful results in a case of epithelioma of the penis in which radium therapy was used. Surface applications were given for ten hours daily over a period of eighteen days. A Columbia paste mold, containing 35 mg. of radium in seven foci, was used. The epithelioma disappeared at the end of three weeks. The technic is described in detail.

RATTNER, Chicago.

LOA-LOA. R. T. BRAIN, Proc. Roy. Soc. Med. **24**:515 (March) 1931.

D. L., a single woman, aged 29, attended Dr. O'Donovan's clinic at the London Hospital on December 17, and gave the following history. Fifteen months before, she went to the coastal area of Nigeria as a missionary. She remained in good health and entirely free from cutaneous disorder until six weeks before coming to the clinic, when a dome-shaped, red swelling, 3 inches in diameter, and raised about ¼ inch, appeared on the left forearm. The swelling was rather tender, but not irritating, and disappeared spontaneously in four days, leaving no trace. Three weeks before, while on the boat returning to this country, she noticed in a mirror a white worm about 1 inch long moving in the skin of the cheek toward the inner canthus of the left eye. As there was no physician on board, she was advised by an experienced passenger to apply pressure to prevent the worm from entering the eye, and when she did so the worm retreated and disappeared. Apart from slight irritation, no local disagreeable sensations were felt during the incident. A week later a painful inflammatory swelling formed in the scalp 1 inch behind the left ear, and broke down discharging a central core like a boil, leaving an ulcer with indurated edges. Ulcers of this type are known to occur in loa-loa, and it was believed that the inflammatory reaction was caused by a dead worm. Examination of the ulcer revealed nothing specific. A blood film (Dec. 17, 1930) showed an excess of eosinophils but no parasites. A good account of loa-loa is given in Manson's "Tropical Diseases," from which the following brief summary is extracted:

"Loa-loa has been known for over three hundred years and is probably of West African origin. It was first described by Guyot in 1778, and in 1891 Manson found a new species of micro-filaria in the blood of two negroes, in one of whom a worm had crossed the eyeball. This newly discovered parasite showed slight morphological differences from *Filaria bancrofti*, and it was only found in the blood during the daytime, so Manson called it *Filaria diurna*. The mangrove fly was suspected of carrying the larval form of the parasite, and after infection of the human subject development was very slow, and adult worms might not appear for from three to five years. In some recorded cases worms have been found 4 to 5 cm. in length and 0.5 mm. thick. They can move 2 to 3 cm. per minute in loose subcutaneous tissues, and occasionally they cross the ball of the eye. It was supposed that the adult worms moved about until fertilization was accomplished, and then the female found a site near a blood-vessel where she deposited ova so that the young filariae could enter the blood stream. Worms have been seen at intervals in a single host for fifteen years. The other peculiar feature of loa-loa is the appearance of Calabar swellings, which arise as painless tumors oval or round, up to 8 cm. in diameter, somewhat inflamed, not pitting on pressure and usually disappearing spontaneously in three or four days."

W. H. GUY, Pittsburgh.

DEMENTIA PARALYTICA IN RURAL POPULATIONS: ITS FREQUENCY AND ETIOLOGIC IMPLICATIONS. A. SÉZARY and A. BARBÉ, Ann. de dermat. et syph. **2**:340 (March) 1931.

The authors addressed a questionnaire to the heads of departmental asylums for the insane and to similar establishments, and from the answers have reached some conclusions concerning the frequency of dementia paralytica in the rural regions of France and the significance of some of the presumed etiologic factors of that disease. It was found that dementia paralytica was rather rare among rural people. In asylums for the insane the number of admissions for this disorder was in proportion to the urban population served. However, the number of persons affected in a department was in relation to the number of syphilitic persons therein. It is only the relative rarity of syphilis in country districts that explains the relative scarcity of dementia paralytica there. It would appear that mental stress and activity (which may be presumed to be greater in city than in country dwellers) is not of any great importance in the etiology of dementia paralytica.

THE DIAGNOSTIC VALUE OF THE REPEATED TUBERCULIN REACTION. H. REISS, Ann. de dermat. et syph. **2**:355 (March) 1931.

Reiss employed the method of Bessau as an indication of the activity of the tuberculous process in ninety patients with tuberculosis of the skin and visceral tuberculosis, and some control cases. In tuberculosis of the skin (chiefly lupus vulgaris and scrofuloderma), 50 per cent gave a reaction indicating an active process; about 14 per cent gave a reaction signifying an inactive condition, and 36 per cent showed a reaction denoting a cachectic state. The number of cases of lupus erythematosus were too few to permit definite conclusions, but all showed a response indicating an inactive process.

The author mentions that the large number of reactions indicating a cachectic state may be explained by the fact that many of these people were of the indigent class, poorly nourished, anemic, etc. Finally, a word of caution about Bessau's method is given. This is, that in increasing the dose of tuberculin to obtain a positive reaction, a nonspecific response may be elicited.

LUPOID "EN PLACARD." A RARE FORM OF BOECK'S DISEASE PROVOKED BY TRAUMATISM AND SIMULATING LEPROSY. N. N. DRACOULIDÈS and B. KÉLÉMÉNIS, Ann. de dermat. et syph. **2**:361 (March) 1931.

In this case, the disease appeared several days after a severe injury. At first there was generalized pruritus followed by large patches, which when seen by the authors, strongly suggested leprosy. However, the rapid evolution, itching, and lack of anesthesia and the results of the laboratory examinations settled the diagnosis.

THE ASSOCIATION OF REDUCING COMPOUNDS AND MERCURIALS IN POMMADES. R. HUERRE, Ann. de dermat. et syph. **2**:367 (March) 1931.

The author, a pharmacist, presents an interesting study of the interaction of various mercurials and certain reducing compounds when incorporated in salves. The reducing substances studied comprised hydroquinone, resorcinol, pyrocatechin, pyrogallic acid and oil of cade.

It was found that cholesterinated petrolatum (3 per cent) was without action on either the mercurials or the reducers. On the other hand, equal parts of petrolatum and hydrous wool fat cause a change in color in pyrogallic acid.

When mixed with any of the reducing substances, the yellow and red mercuric oxide and the basic sulphate are rapidly transformed with a change in color into the black mercuric oxide or into a mixture of the oxide and basic sulphate. However, the red and black sulphide, the oxide and elemental mercury are not modified when mixed with the aforementioned reducing substances and oil of cade.

HISTOGENETIC AND PATHOGENETIC INTERPRETATION OF KAPOSI'S SARCOMA. L. HUDELO and F. CAILLIAU, Ann. de dermat. et syph. **2**:417 (April) 1931.

Hudelo and Cailliau have studied a case of this disease that came to necropsy. The tissue was stained by special stains (Masson, Bielschowsky, etc.), and the results of the examination are discussed especially in the light of the recently advanced idea of Pautrier that the disease is not a sarcoma.

The authors give a detailed description of their histologic studies, which led them to the conclusion that Kaposi's disease is not a sarcoma. While its angiomatous feature is a dominant characteristic, it does not seem to be the initial lesion, which is a proliferation of the cells of Schwann in the vessels. Kaposi's sarcoma has many analogies to von Recklinghausen's disease.

Hudelo and Cailliau, in contradistinction to Pautrier, found no evidence of true vascular glomi or of tactile corpuscles. In discussing the angioneuromatous aspect of Kaposi's disease, the authors consider that it may be determined by one of three mechanisms: (1) the metaplasia of muscle fibers into nerve cells; (2) combined proliferation of muscle and nerve elements, and (3) an exclusive and primary origin from nerve cells. They favor the last hypothesis. Finally, having noted definite pathologic changes in the endocrine glands at necropsy, the authors mention the possibility that the endocrine-autonomic apparatus may play a rôle in the disease.

PRIMARY ALOPECIA OF HEAD-BAND CONFIGURATION. R. SABOURAUD, Ann. de dermat. et syph. **2**:446 (April) 1931.

After discussing the fall and regrowth of hair, Sabouraud describes a rare form of alopecia of which he has seen not more than a dozen cases in thirty years. All his patients were females, chiefly of mature years. In two cases he has seen the early stages which consisted of a triangular area of alopecia above and in front of the ears. These areas are later joined by a narrow band of alopecia extending from side to side just within the anterior hair line. The early stages show crust formation followed by permanent baldness due to follicular atrophy. Once established, the condition does not seem to spread. In one early case, Sabouraud arrested the process by the use of an ointment containing tar, sulphur, pyrogallic acid, red mercuric bisulphide and resorcinol, the formula for which is given. No opportunity for histologic study has presented itself.

COMMENTS ON CRYOTHERAPY. L. LORTAT-JACOB and G. SOLENTE, Ann. de dermat. et syph. **2**:461 (April) 1931.

The authors mention that Pusey recently remarked to them that cryotherapy had two important features in its favor; its innocuousness and the numerous disorders in which it was of value. However, success with the method depends on careful attention to the technic of application. In tuberose angiomas, it has no superior. In plantar warts, the authors prefer it to any other method of treatment and in hypertrophic scars and senile keratoses it has no rival. The authors also employ it in rhinophyma, leukoplakia, xanthelasma and seborrheic warts.

INVESTIGATION OF INFANTILE ECZEMA. M. and MME. H. MONTLAUR, Ann. de dermat. et syph. **2**:513 (May) 1931.

The research of the Montlaurs was on the type of infantile eczema that has been called the seborrheic variety. The lesions first appear on the buttocks, and involve the folds; they spread upward and downward in the form of large patches partially moist and partially dry with a loose scale which after desquamation leaves an attached fringe along the periphery of the patch. The disease begins early, from the first to the sixth week of life. In extensive cases the face and scalp may be invaded, the scalp showing a heavy "milk crust," and the face large patches with greasy crusts.

Cultures from the scales and surfaces of the lesions in various mediums always gave an abundance of enterococci. In the infants' stools, the enterococcus was found abundantly, while the colon group of bacteria were in eclipse; this is the reverse of normal conditions. The stools likewise gave evidence of increased fermentation. Streptococci were rarely, if ever, found in the dermal lesions. An intradermal test for streptococcic allergy in thirty-two cases gave negative results in all but two, and these infants gave feebly positive reactions. Injection of enterococcic vaccine in some cases produced lesions resembling the natural disease. This vaccine has given beneficial therapeutic results which will be reported in a subsequent paper.

ATROPHIC AND CONGENITAL ROSEOLA WITH HISTIOCYTIC INFILTRATION. CHATELLIER and IZARD, Ann. de dermat. et syph. **2**:534 (May) 1931.

The authors report a case of a condition that seems to be hitherto unrecorded. A young man exhibited a generalized eruption composed of faint pink, slightly raised nummular patches. At some distance the resemblance to a secondary roseolar syphilid was marked. The disturbance had been present since infancy. A biopsy showed as its most prominent feature an infiltration, in smaller or larger masses, composed of basophilic and metachromatic cells containing granules. These cells appeared to belong to the histiocytic series.

THE ASSOCIATION OF CUTANEOUS TUBERCULOSIS WITH THAT OF OTHER ORGANS. N. C. VAN VONNO, Ann. de dermat. et syph. **2**:543 (May) 1931.

The author's views rest on a clinical study of 253 cases of various types of tuberculosis of the skin. These cases were examined especially in regard to the coexistence of visceral manifestations of the disease. Van Vonno states that any evidence on this point must be advanced with some reserve, since tuberculous foci are sometimes impossible to detect during life. He entirely rejects the idea of esophylaxis of Hoffman, at least as regards tuberculosis. He is firmly convinced that tuberculosis of the skin (except tuberculosis verrucosa cutis) is rarely primary in the skin. The most important source of cutaneous contamination is the lymphatic system. In his cases, 72 per cent of the patients showed involvement of the lymph nodes. The author also believes that the lymph glands produce tuberculous antibodies. The resistance of the skin to tuberculous infection is a result of antibodies formed in the lymph nodes. As a practical point, the author mentions that he always applies roentgenotherapy to the regional lymphatics in cutaneous tuberculosis.

ECZEMA OF EXPOSED AREAS DUE TO STREPTOCOCCUS. H. JAUSION, G. LARTIGUE and A. SLIOSBERG, Bull. Soc. franç. de dermat. et syph. **38**:417 (March) 1931.

The authors encountered a severe vesicular dermatitis of the face and neck which followed impetigo contagiosum. They were at first inclined to consider photosensitization as the etiologic background, but finally convinced themselves, chiefly by biologic reactions, that the disorder was of streptococcic origin.

PRURIGO PROVOKED BY LIGHT. H. JAUSION, G. LARTIGUE and A. SLIOSBERG, Bull. Soc. franç. de dermat. et syph. **38**:423 (March) 1931.

The patient presented a pruriginous eruption of the face and neck. It was composed of numerous prurigo-like papules. For a number of years a similar attack had appeared at the beginning of Spring. No provoking cause could be determined by the history. There was a positive Prausnitz-Kustner reaction to lysed streptococci. After this reaction had subsided, exposure of its site to artificial light approximating the spectrum of sunlight produced a reactivation. The eruption disappeared after a short course of "clasine streptococcique" injections. The authors think that in this case streptococcic toxins acted as the antigen pro-

ducing a terrain abnormally reactive to sunlight. Similar conditions probably account for several other dermatoses, i. e., a combination of a sensitized soil produced by bacterial toxins plus light.

INVESTIGATION OF ACNE VARIOLIFORMIS. MILIAN, Bull. Soc. franç. de dermat. et syph. **38**:438 (March) 1931.

Milian saw a patient with this disease in which a culture yielded *Staphylococcus albus*. When this organism was injected into rabbits, it produced a dry black eschar with several satellite lesions clinically similar to acne varioliformis. The result demonstrated that *Staphylococcus albus* was pathogenic and that when injected into rabbits it produced a lesion analogous to acne varioliformis.

PHAGEDENIA OF THE PENIS: CULTURE OF PATHOGENIC STAPHYLOCOCCUS, CURE BY AUTOVACCINE THERAPY. P. CHEVALLIER, LÉVY-BRUHL and R. MORICARD, Bull. Soc. franç. de dermat. et syph. **38**:448 (March) 1931.

From a patient with a mixed phagedenic chancre, the authors isolated a staphylococcus which had a high virulence for laboratory animals. A vaccine of this organism produced a rapid cure of the phagedenic element.

A CASE OF NICOLAS-FAVRE DISEASE VERIFIED BY INOCULATION OF A MONKEY. C. LEVADITI, M. PINARD and P. ROBERT, Bull. Soc. franç. de dermat. et syph. **38**:455 (March) 1931.

This patient presented inguinal adenitis which had been preceded by a small, spontaneously healed penile ulcer. He was first treated for chancroid, then for syphilis, but without effect on the adenitis. Finally, a monkey was inoculated with tissue juice from the affected glands, and an intense meningo-encephalitis developed. The authors apparently considered this result as demonstrative of poradenitis, but this conclusion was challenged by Ravaut (in the discussion) who remarked that it only proved that there was a virus pathogenic for monkeys in some human bubos.

TWO CASES OF SEROLOGICALLY NEGATIVE PRIMARY SYPHILIS TREATED EXCLUSIVELY BY BISMUTH. L. QUEYRAT, Bull. Soc. franç. de dermat. et syph. **38**:458 (March) 1931.

In both these cases, an oil-soluble preparation of bismuth was used; four courses of twenty injections each were given during the first year of treatment (total dose 6.4 Gm. of elemental bismuth). Throughout the course of treatment the serum remained negative, and at the end of the period the patients were clinically cured. Queyrat presented these cases as evidence of the efficacy of bismuth, which he now prefers to the arsphenamines in the treatment of syphilis.

KERATODERMA DUE TO GOLD THERAPY. R. RABUT, Bull. Soc. franç. de dermat. et syph. **38**:463 (March) 1931.

The case reported by Rabut seems to be unique. His patient had received nine injections of a gold compound when a generalized erythema developed accompanied by systemic symptoms. The erythema was followed by a pronounced desquamation and keratodermic areas.

ULCERATIVE PYODERMAS OF SYPHILITIC ASPECT. L. HUDELO and R. RABUT, Bull. Soc. franç. de dermat. et syph. **38**:464 (March) 1931.

Hudelo and Rabut report three cases of ulcers of the legs having a polycylic configuration and strongly suggesting a syphilitic origin. They all began, however, in superficial, banal, pyodermic lesions. Cultures from the lesions revealed only staphylococcus.

EXFOLIATIVE DERMATITIS FROM NEOARSPHENAMINE: AUTOHEMOTHERAPY FOLLOWED BY FURUNCULOSIS; BIOLOGIC TESTS FOR SENSITIZATION TO NEOARSPHENAMINE. J. GATÉ, H. THIERS, J. CHARPY and P. CUILLERAT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyons) **38**:400 (March) 1931.

The authors record a case in which the patient received an intensive course of injections of neoarsphenamine. A widespread erythematosquamous and vesicular dermatitis developed with severe systemic symptoms. The dermatitis was favorably influenced by autohemotherapy, but a large number of furuncles appeared. By inoculation into guinea-pigs, successful passive transfer of arsphenamine sensitivity was demonstrated with the patient's blood. The fact that furuncles developed despite autohemotherapy, which in France apparently is recognized as usually efficacious in that disorder, is not surprising since injections of whole blood are most valuable in boils due to internal causes.

ANORECTAL STRICTURE WITH POSITIVE FREI'S REACTION. J. NICOLAS, M. FAVRE, G. MASSIA and F. LECAT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyon) **38**:406 (March) 1931.

Another case of the disorder formerly called anorectal syphiloma (Fournier) is reported in which Frei's reaction for poradenitis was positive. The disorder had been present six years, and the patient was syphilitic. Histologic examination showed the features of poradenitis.

EXFOLIATIVE DERMATITIS FOLLOWING TREATMENT BY A GOLD SALT. CAUSSADE and DROUET, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **38**:332 (March) 1931.

After four injections of gold and sodium thiosulphate, the patient developed systemic symptoms of intolerance and a generalized erythroderma which endured about two months. The authors briefly consider the manifestations of intolerance to gold compounds and conclude that caution must be exercised in its use. One should begin with small doses and always watch for signs of sensitivity.

PAPULOSQUAMOUS TUBERCULIDS CURED BY GOLD THERAPY. CAUSSADE and DROUET, Bull. Soc. franç de dermat. et syph. (Réunion dermat., Nancy) **38**: 335 (March) 1931.

The authors record a rapidly successful result with injections of a gold compound in a case of tuberculids. The patient had definite indications of active pulmonary tuberculosis, and the therapy appeared to have a favorable influence on the general state.

DUHRING'S DISEASE IN A CHILD WHOSE MOTHER HAD TERTIARY SYPHILIS. SPILLMANN, WEIS and SEGALL, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **38**:355 (March) 1931.

The case recorded is that of a boy of 4 years who had a typical dermatitis herpetiformis. The mother had tertiary syphilis. The child, who had no clinical or serologic evidence of syphilis, was given sulpharsphenamine with disappearance of the eruption in about one month. The authors report the case without implications.

VARIATIONS IN THE ACID-BASE BALANCE IN SOME DERMATOSES. SPILLMANN, VERAIN and WEISS, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **38**:364 (March) 1931.

While admitting the importance of the conception of allergy in the etiology of eczema, the authors do not believe that all cases of that disease are of allergic origin. For some years they have been studying the acid-base balance in several

diseases (eczema, prurigo, urticaria, psoriasis) and reported their results in the *Annales de Dermatologie et Syphiligraphie* (**10**:1301[Dec.] 1929). In the present report they record examinations in 116 new cases. They employed an electrometric measurement of the blood p_H.

Of 80 cases of eczema, 60 showed alkalosis, 4 normal figures and 16 acidosis. Of 16 cases of psoriasis, 12 showed alkalosis, 1 normal figures and 3 acidosis. Of 3 cases of urticaria, 2 showed acidosis and 1 alkalosis. Four cases of dermatitis seborrheica showed alkalosis and 1 acidosis. Five cases of pruritus cutaneous and prurigo showed alkalosis and 2 acidosis. One case of Duhring's disease gave alkalotic figures, the other acidotic. Two cases of erythroderma (not qualified) showed alkalosis and 1 acidosis.

From this study, it is concluded that an acid-base imbalance is present in certain skin diseases that are regarded as cutaneous reactions. It plays an especially prominent rôle in those having an exudative feature (eczema particularly). The imbalance may be either toward the acid side (22 per cent) or the alkalotic (73 per cent). The degree of imbalance varies with the case rather than with the intensity of the eruption, except that in each case there appears to be a close relation between fluctuations in the acid-base disequilibrium and the clinical course. There were, however, some exceptions to this general rule. From the therapeutic standpoint, those cases showing acidosis were most amenable to therapy directed toward the p_H imbalance. The alkalotic cases were less influenceable.

In general, it may be concluded that an acid-base disequilibrium is one of the features of a dermatopathic terrain. It is not a question of whether there is an acidosis or alkalosis but whether there is a derangement of the acid-base balance.

FOX-FORDYCE DISEASE. F. WORINGER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:297 (March) 1931.

A typical case of Fox-Fordyce disease was presented. It has been noted by Pautrier that pruritus always precedes the objective manifestations. The condition in this case did not respond to ovarian extract, though success with this measure has been reported in some cases.

APLASIA MONILIFORMIS. L. M. PAUTRIER and R. GLASSER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. Strasbourg) **38**:305 (March) 1931.

The unusual feature about this otherwise typical case in a child of 11 years was that it was the first occurrence of the disorder in the family.

ACQUIRED STELLATE TELANGIECTASES (DEVELOPING DURING PREGNANCY) LIMITED TO THE UPPER PART OF THE RIGHT ARM IN THE AREA OF THE DISTRIBUTION OF THE CERVICAL PLEXUS. L.-M. PAUTRIER and A. ULLMO, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:309 (March) 1931.

The patient, who had been pregnant twice before, noted the lesions at the beginning of her third pregnancy. They occurred on the upper part of the right arm; there were a few lesions on the neck, left arm and nose. Surrounding the telangiectases was a narrow zone of partly or completely achromic, atrophic skin. The appearance of this disorder in pregnancy seems to have been noted in but one other case, that of Zeisler.

TREATMENT FOR PRURITUS VULVAE ET ANI BY RADIATION OF THE SYMPATHETIC GANGLIA. J. GOUIN and A. BIENVENUE, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:323 (March) 1931.

In cases of pruritus vulvae et ani that were manifestly not of external origin, the authors have irradiated the lumbar region of the spine. In many cases a

transitory exacerbation occurs. Vulval pruritus, if associated with menstrual or other utero-ovarian disturbance, was especially responsive. Only those cases associated with asthma proved recalcitrant.

URTICARIA DUE TO COLD. L.-M. PAUTRIER and A. ULLMO, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:329 (March) 1931.

Pautrier and Ullmo report a case of urticaria due to cold in which examination showed lowered blood pressure, diminution of leukocytes and slight increase of large mononuclears before the attack. Because of the refusal of the patient, they could not determine whether these symptoms of shock preceded or accompanied the urticarial outbreak.

MICHAEL, Houston, Texas.

IODOFORM IDIOSYNCRASY. E. BIZZOZERO and A. V. FERRARI, Gior. ital. di dermat. e sif. **72**:3 (Feb.) 1931.

The study of a case of iodoform idiosyncrasy in a young man suffering from lupus vulgaris, led the author to the following conclusions:

The cutaneous reaction appears only when the drug is placed in contact with the epidermis. There is no reaction when iodoform is placed on the denuded dermis or in the mucous membranes. The probable seat of the reaction is in the stratum granulosum and in the stratum lucidum.

Idiosyncrasy to iodoform is due to a hypersensibility to the alkaline radical derived from methane, when iodized, and to the number of atoms of H in the molecule.

The presence of a reagin in the serum of the patient can be demonstrated in from ten to twenty minutes after the reaction takes place. Passive idiosyncrasy may be demonstrated by the method of Prausnitz and Küstner.

It is proved that idiosyncrasy to iodoform is the result of conflict between the allergen and a specific reagin.

INFLUENCE OF ULTRAVIOLET RAY, X-RAYS, RADIUM AND OTHER METALS ON THE WASSERMANN REACTION. A. AMBROGIO, Gior. ital. di dermat. e sif. **72**:75 (Feb.) 1931.

The author concludes that these physical agents, as well as cobalt and nickel, have no influence on the results of the Wassermann test.

ACHROMATIC EPIDERMOMYCOSIS DUE TO HEMISPORA STELLATA. G. MANTARRO, Gior. ital. di dermat. e sif. **72**:130 (Feb.) 1931.

The author reports six cases of a peculiar macular and achromatic dermatosis found in young people who had been exposed to the sun. He found mycelia in the scales, the cultures proving it to be a fungus of the type *Hemispora stellata*. The condition seems to be a primitive epidermomycosis which is made more apparent, when, after exposure to the sun rays, there is a certain amount of pigmentation of the surrounding skin and contrasting achromia on the infected spots.

This condition reported by Mantarro may be identified with that described by the reviewer in ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**9**:82 [Jan.] 1924) under the name of achromia parasitaria.

CYSTIC LYMPHANGIO-ENDOTHELIOMA OF THE SCROTUM. M. BORTOLOZZI, Gior. ital. di dermat. e sif. **72**:144 (Feb.) 1931.

The author reports a case of cystic lymphangio-endothelioma of the scrotum in a man, aged 66. The description of the tumor and the colored histologic drawings are excellent. Bortolozzi found numerous muscular fibers, lymphoid nests and giant cells among many microcystic lymphangiectasia. The lesions resembled those of tuberculosis in some respects.

PARDO-CASTELLO, Havana.

THE HYDROGEN ION CONCENTRATION OF THE SURFACE OF THE SKIN IN VARIOUS DERMATOSES. A. PERUTZ and B. LUSTIG, Arch. f. Dermat. u. Syph. **163**:18 (March 30) 1931.

The hydrogen ion concentration, or p_H, of the skin was determined on the water soluble constituents of the surface by means of Wolff indicator sheets. This method had been previously shown to give results which coincided with those of Schade and Marchionini made with a potentiometer.

A number of cases of acute, subacute and chronic eczema, acne vulgaris, dermatomycosis, prurigo, pruritus and psoriasis were examined. Changes in the p_H were found only in a few cases and only in those in which the uppermost epithelial layer was gone, resulting in a moist lesion. In such cases the reaction, while still remaining slightly acid, was less so than that of the normal skin, showing a shifting of the reaction toward the alkaline side.

The pharmacologic action of solution of aluminum acetate, N. F., is declared to be based on the fact that its p_H is almost isotonic with that of normal skin and because of its buffer action is able to shift an abnormal p_H reaction of the skin back to the normal value.

RELATIONSHIP OF CONDYLOMATA ACUMINATA TO CARCINOMA OF THE PENIS. A. BUSCHKE and L. LOEWENSTEIN, Arch. f. Dermat. u. Syph. **163**:30 (March 30) 1931.

Condylomata acuminata of the penis may grow very rapidly and clinically resembles carcinoma. A biopsy is often necessary to establish the diagnosis. Two cases are described in which condylomata acuminata on the penis were precancerous lesions leading to microscopically proved carcinoma.

PATHOGENESIS OF TINEA OF THE HANDS AND FEET. AUGUST MATRAS, Arch. f. Dermat. u. Syph. **163**:47 (March 30) 1931.

This paper is primarily a discussion of the theory of epidermophytids occurring on the hands secondary to tinea infections of the feet, a possibility first suggested by Williams. The author has examined sixty-seven cases of tinea in which lesions were simultaneously present on the hands and feet. Eight showed positive findings on the hands. Twenty of the cases, or 30 per cent, gave a negative reaction to tricophytin (1:50 Hoechst tricophytin). Because of these findings, the author is inclined to consider many cases of lesions on the hands occurring in conjunction with lesions on the feet as being due to direct infection and not as secondary dermatophytids.

MONASH, New York.

A CASE OF LUPUS VULGARIS WITH PARTICULARLY STRIKING SPECIFIC GENERAL AND LOCAL REACTION. KLEMENS KAUCZYŃSKI, Dermat. Wchnschr. **92**:525 (April 11) 1931.

A patient, aged 28, who had been under treatment for an extensive lupus vulgaris of the head, neck, trunk and extremities was found to have a positive Wassermann reaction. She received considerable antisyphilitic therapy, including arsphenamine, bismuth and iodide. Subsequently therapy with the Finsen light provoked a severe general reaction with elevated temperature, chills, etc., and in addition, a marked local reaction in the lesions consisting of extravasation of blood and areas of necrosis. The reaction cleared, and further therapy with the Finsen light did not provoke any further reaction.

THE PROBLEM OF LUPUS IN SOUTHERN HUNGARY. K. v. BERDE, Dermat. Wchnschr. **92**:529 (April 11) 1931.

The author reviews the available statistics of lupus vulgaris for his part of the country and finds the disease somewhat more frequent there than elsewhere. Fifty per cent of the patients seen in the clinic in Szeged did not return a second time, and this fact indicates the difficulty in coping with the condition.

THE OCCURRENCE OF THE LUETIN REACTION IN CONGENITAL SYPHILIS. THERESE KINDLER, Dermat. Wchnschr. **92**:538 (April 11) 1931.

"Luotest," a luetin prepared by Müller and Brandt from the testes of syphilitic rabbits, was used in 103 cases of congenital syphilis. In the first year all tests were negative; between the first and fourth year, 25 per cent were positive; from the fourth to the fourteenth year, 93 per cent; from the fourteenth to the twentieth year, 80 per cent, and beyond the twentieth year, 83.3 per cent were positive. The test is considered a valuable addition to the Wassermann reaction in this type of syphilis.

IS EPIDERMODYSPLASIA VERRUCIFORMIS (LEWANDOWSKY-LUTZ) AN INDIVIDUAL DERMATOSIS? L. N. MASCHKILLEISSON, Dermat. Wchnschr. **92**:569 (April 18) 1931.

The cases previously reported (twenty-one) are listed in tabular form. The author describes a typical instance in a patient 23 years of age in whom the cutaneous condition first appeared when he was 2 years old. The histology is described. A second case is reported in which the eruption was limited to the forehead and in which the histology was similar to that of the typical case of epidermodysplasia. The author concludes: 1. This condition is distinct from the verrucae. 2. It belongs to the group of skin dystrophies, connected with the precancerous conditions. 3. The histologic characteristic is "clear degeneration" of isolated areas of the upper epidermis, a phenomenon quite distinct from parenchymatous edema.

LINEAR ECZEMA OVER AN ACUTE LYMPHANGITIS. W. LUTZ, Dermat. Wchnschr. **92**:578 (April 18) 1931.

In a laboring man, aged 50, with a pyodermia of the fifth finger, a scaly eczema developed over the linear lymphangitis extending from the middle of the arm to the middle of the forearm. The eruption cleared up and the underlying lymphangitis disappeared as the patient was cured of pyodermia.

CONTRIBUTION TO THE KNOWLEDGE OF LYMPHOGRANULOMA INGUINALE. ALFRED COHN and LUDWIG KLEEBERG, Dermat. Wchnschr. **92**:580 (April 18) 1931.

Repeating the experiments of Hellerström and Wassén, the authors were unable to infect an ape with lymphogranuloma inguinale by intrapreputial injection of material from an infected lymph node. Intracerebral injection caused a fatal outcome, and material from the meninges, sterilized at 60 C. for three hours on two successive days, produced skin reactions in five patients with lymphogranuloma but none in normal controls.

L. TAUSSIG, San Francisco.

DATA ON THE DIAGNOSIS OF FOX-FORDYCE DISEASE. JOZSEF ZOLLSCHAN, Borgyogyaszati Szemle **9**:31 (Feb.) 1931.

Fox-Fordyce disease is considered a disease entity, separate from both the "lichen simplex chronicus Vidal" group and the "neurodermitis chronica circumscripta" group of Jadassohn, Broque and Arndt. The author describes two specifically localized neurodermites and calls attention to their response to x-ray therapy. In these locations are found the Schieferdecker apocrin sweat glands which have a common opening with the follicles in contrast to the normal "Ekkrin" sweat glands which do not communicate with the openings of the follicles. The apocrin glands are larger than the "Ekkrins," and their secretion is different. They have some connection with the sex cycle since they function only after puberty, and their function reaches a maximum during menstruation and during pregnancy.

H. C. SCHORR, Chicago.

STUDIES ON THE CONSTITUENTS OF THE SPIROCHETE: II. ON PROTEINS IN SPIROCHETES. H. SAWADA, Lues: Bull. Soc. japon. de syph. **5**:257 (Dec.) 1930.

Investigations by the author made it seem probable that nucleoproteids are contained only in *Spirochæta recurrens* and not in *Spirochæta pallida*. Basic proteins, however, were found in both.

METASTATIC LESIONS DUE TO INTRAVENOUS INJECTIONS OF SPIROCHÆTAE PALLIDAE. M. HASHIGUCHI and N. KATO, Lues: Bull. Soc. japon. de syph. **5**:264 (Dec.) 1930.

The authors have infected rabbits intravenously with an emulsion of syphilitic virus and produced generalized papules, orchitis, epididymitis, lesions in the nasal and vertebral bones and keratitis parenchymatosa. They did not find any spirochetes in the liver, kidney, spleen and heart. This intravenous method enables one to produce generalized lesions readily in 100 per cent of the rabbits, provided the experiment is performed under most favorable conditions. The studies in which the generalized lesions are taken as indication are, according to the authors, by no means less valuable in various phases of pathologic and immunologic researches in syphilis than the studies in which the local lesions have been made the only indication of the experimental syphilis.

THE "HEMATO-ENCEPHALIC BARRIER" IN SYPHILIS. ZENSETSU OHYA, Lues: Bull. Soc. japon. de syph. **5**:280 (Dec.) 1930.

In twenty-three cases of neurosyphilis the authors have studied the "hemato-encephalic barrier" by means of the hemolysin reaction of Weil and Kafka. Three cases showed hypofunction of the barrier: an increase of the meningeal permeability. In two of these three cases there were a number of syphilitic changes in the cerebrospinal fluid, but in the third case the Bordet-Wassermann and the Sachs-Georgi reactions were negative. In the other twenty cases the function of the barrier was normal in spite of a marked syphilitic change in the cerebrospinal fluid. The same experiment carried out on three healthy persons showed no change in the hemato-encephalic barrier by the hemolysin test of Weil and Kafka.

BLOOM, New York.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

MONILIA VULVOVAGINITIS. E. D. PLASS, H. C. HESSELTINE and I. H. BORTS, Am. J. Obst. & Gynec. **21**:320 (March) 1931.

According to Plass and collaborators, *Monilia* is frequently present in the vaginal secretions of patients with vulvovaginitis and appears to be concerned directly with the etiology of the clinical condition, although normal individuals may harbor the fungi for long periods without showing vaginal irritation. Pregnancy and diabetes are definite predisposing factors, and menstruation may be, since sexually active women are more prone to the infection. Parous women are more often infected, but children, virginal adults and senile women may likewise show the organisms. In the majority of instances the mode of infection cannot be demonstrated. High acidity of the vaginal secretion favors the growth of *Monilia* but is not essential. The chief symptoms of the infection are itching, burning and smarting of the lower vagina and vulva. Digital and speculum examinations, and coitus are painful. A profuse leukorrhea rarely appears, and only occasionally is the secretion characteristic, when it contains small white flakes of thrush-like

material. Varying degrees of vaginitis are encountered, with, occasionally, the appearance of denite vaginal or cervical thrush. Complications are rare. *Monilia* vaginitis tends to undergo spontaneous relief, but occasionally becomes chronic and may produce recurrent irritation over a period of months or years. Delivery usually leads to complete relief in pregnant women, while menstruation generally has the same effect temporarily in the nonpregnant. Gentian violet, in 1 per cent aqueous solution, applied locally affords the best method of treatment. Alkaline douches may be of some value. *Monilia* vaginitis in pregnant women is a definite source of infection in sporadic outbreaks of oral thrush in the new-born.

PENETRATION OF LIGHT THROUGH HUMAN SKIN. A. BACHEM and C. I. REED, Am. J. Physiol. **97**:86 (April) 1931.

Bachem and Reed state that visible and near infra-red rays are strongly absorbed by the blood of the corium and subcutaneous layers, with direct effects on the blood to be expected. The heating effect must be rather mild on account of the small absorption in the epidermis and the strong convection by the blood stream. The far infra-red has little penetrating power. Most of it is absorbed in the epidermis. The heat produced is slowly conducted away by the blood stream and by the air. Overexposure of the germinal layer may lead directly to blistering. There is greater variation in percentage penetration of ultraviolet than in other parts of the spectrum. At 280 millimicrons the absorption in the corneum and prickle-cell layers is pronounced. The great antirachitic effect of this wavelength must occur in or about these layers. On both sides of this band, near 300 and 250 millimicrons, the penetration is greater, more radiation reaching the stratum malpighii and the corium. These observations indicate that erythema production occurs in the germinal layer (or the corium) under the shadow of the upper layers. The stratum corneum and granulosum must play an important part in the light protection of these sensitive layers. From 250 millimicrons down the absorption in the horny layer increases rapidly. Near 200 millimicrons the absorption is so complete as to prevent any radiation from reaching the living layers of the skin.

CLINICAL VALUE OF COMBINED KAHN AND WASSERMANN TESTS IN TROPICS WITH SPECIAL REFERENCE TO YAWS AND SYPHILIS. H. J. O. BURKE-GAFFNEY, J. Hyg. **31**:215 (April) 1931.

Burke-Gaffney tested serums from 500 patients, mostly natives of East Africa, by the Kahn and Wassermann tests. Clinical data were available in the case of 448 specimens. The results of tests on 230 serums from cases believed to be yaws and syphilis and 218 cases believed not to be yaws and syphilis are discussed. In 46 of the 230 cases, treatment had previously been given. In interpreting the results, the resolutions of the League of Nations conference on the serodiagnosis of syphilis were strictly followed. In the performance of the tests, recognized standard methods were used. The two tests correlated exactly in 96.4 per cent of all cases. The Kahn test was the more sensitive to yaws and syphilis. The Wassermann test alone gave one nonspecific reaction. The reagents used in the Kahn test did not deteriorate when kept for two months at room temperature. It is suggested that, although the use of both tests is preferable when practicable, the Kahn test alone is a reliable diagnostic measure in the tropics.

BOILS AND CARBUNCLES AMONG MINERS. S. W. FISHER, Lancet **1**:750 (April 4) 1931.

Fisher believes that, as far as mines are concerned, boils do not present a serious problem, except in a few isolated cases, and that the main factor in the causation of boils underground is a high wet bulb temperature, which at one and the same time indicates suitable conditions (warmth and moisture) for the vitality of the organism and opens the sweat glands and hair follicles and thus facilitates the entry of the staphylococcus.

Fifth Disease (Epidemic Erythema Infectiosum). A. Pinelli, Pediatria **39**:248 (March 1) 1931.

Pinelli reports ten cases of epidemic erythema infectiosum (the so-called fifth disease), a contagious, autochthonous and specific infection which attacks children, mostly between 3 and 8 years. Nurslings are not attacked even though they may continue to live with the infected children. The contagion takes place by the transmission of the virus through direct contact of infected children with normal children. The clinical picture of the disease in its several stages (incubation, appearance, generalization and disappearance of the exanthem) is described. During the stage of generalization the skin seems as if infiltrated, and in grave forms it has an erysipelatous appearance. During the presence of the disease, changes in the hematologic picture are observed. The cutaneous exanthem is neither preceded nor associated with severe general phenomena. It presents special characteristics which differentiate it from any other form of exanthem. When the exanthem disappears, no desquamation takes place. The prognosis of the disease is good. All patients observed by the author recovered without any complications or sequelae and without having received any special treatment.

Bacteriophage Therapy in Localized Pyogenic Infections. G. Pacetto, Policlinico (sez. chir.) **38**:76 (Feb. 15) 1931.

Pacetto applied bacteriophage therapy in thirty-six cases of furuncles, carbuncle, hidrosadenitis, abscess, phlegmon and mastitis. In 88.2 per cent of the cases a cure was effected in from two to ten days, with from one to three injections of bacteriophage. In 11.8 per cent of the cases the suppurative process resisted the bacteriophage and surgical intervention became necessary. In no case did exacerbation result from the bacteriophage therapy.

Dietary Therapy of Lupus and Other Skin Diseases. G. Stümpke and B. H. U. Mohrmann, Med. Klin. **27**:235 (Feb. 13) 1931.

By way of introduction, Stümpke and Mohrmann review the results which other workers obtained with the Gerson-Sauerbruch-Herrmannsdorfer salt-free diet. They themselves employed it in fifteen cases of lupus vulgaris. In ten of these cases they saw a favorable influence. In three instances there was no effect to be seen, in spite of the fact that the treatment had been continued for a considerable time. In two boys, aged 10 and 13 years, respectively, exacerbation was noted during the dietary treatment. The authors think that in the infantile organism the salt-free diet has a different mode of action than in the adult organism. The infantile organism has a greater avidity for sodium chloride, probably because it requires it for the growth process. In the conclusion it is stated that even in those cases in which the diet had a favorable influence the cure was not complete. The authors think that the dietary treatment is helpful in combination with other therapeutic methods but that it cannot be considered as the method of choice or as the inauguration of a new era in lupus therapy. In regard to other forms of dermatoses, it is stated that the salt-free diet was employed in all in about eight cases. However, among these there were many in which the dietary treatment was not employed alone but in combination with other therapeutic measures, and for this reason the results obtained cannot be entirely ascribed to the salt-free diet. With the exception of neurodermatitis and pemphigus, which are otherwise difficult to influence, there is no definite reason for extensive application of dietary therapy in skin diseases.

Action of Light on Bacteria. O. Winterstein, Strahlentherapie **39**:619 (Feb. 21) 1931.

Winterstein's tests have confirmed the observation that ultraviolet rays are able to impair the growth of pathogenic and nonpathogenic bacteria or to destroy them. Young cultures proved to be more sensitive to the rays than old cultures. The resistance differed in bacterial individuums of the same culture and in various

strains of homogenous bacteria; moreover the resistance appeared to be different in various bacterial species. The growth of fresh and of six hours old cultures was impaired by a dose of rays below or about that causing erythema in the abdominal skin. A dose of about or above that causing erythema was fatal for fresh cultures, while a dose causing severe burns was necessary for destruction of cultures six hours old. A dose of rays causing erythema of the abdominal skin proved fatal for streptococci; a much larger dose, namely, such as causes injury of the tissues, was necessary for destruction of *Staphylococcus aureus* and *Bacillus coli.* The resistance of tubercle bacilli proved to be twice as great as that of staphylococci. No connection was found between the resistance of bacteria to acids and that to light. It appeared that the visible and the ultraviolet rays have no amitokinetic action. Bacteriophages displayed a notable sensitiveness to the rays. Ferments appeared to resist the rays better than did bacteriophage. A clinical dose of ultraviolet rays was able to destroy a large number of bacteria, chiefly of nonpathogenic bacteria, suspended in the air or present on the ground and on the surface of objects. In the air experimentally infected with colon bacilli, streptococci and staphylococci, the microbes remained for hours when the weather was dry, while damp weather appeared to favor their settling on the ground. Bacteria proved to survive in dried and pulverized garden earth exposed to ultraviolet rays. The rays were able to destroy a large number of bacteria present on the human skin; the necessary dose was well tolerated by the hands and forearms but caused burns on the abdominal skin. The clinical dose of rays was unable to destroy bacteria in wounds, nor could the rays destroy pneumococci and streptococci present in pus. Rays cannot be used for sterilization of suture threads, because their action is superficial; they do not destroy bacteria present within the threads. Evidently the visible, and especially the ultraviolet rays, appear to cause changes in the protein structure of the bacterial protoplasm resulting in impairment of growth and destruction of bacteria. Large doses of rays were able to destroy antibodies. Sensitization to light, namely to visible rays, appeared possible by means of fluorescigenous dyes. The author emphasizes that the therapeutic value of artificial ultraviolet rays ought not to be overestimated.

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

M. B. Parounagian, M.D., *Secretary*

Regular Meeting, Jan. 13, 1931

Jerome Kingsbury, M.D., *Chairman*

Dermatitis Artefacta? Presented by Dr. Max Scheer.

B. L., a woman, aged 21, from the New York Post-Graduate Clinic, presented an oval-shaped, bean-sized, erythematous area covered with thin cigaret paper-like scales, in the region of the left anterior axillary fold. The lesion was slightly atrophic. The patient stated that the lesion had appeared about three years prior to presentation and had persisted, unaltered in any way.

DISCUSSION

Dr. George C. Andrews: I have the impression that the condition is neurodermatitis. The patch is linear and itches, and she says that she has rubbed it for three years.

Dr. Fred Wise: I do not accept the diagnosis of artificial or self-inflicted dermatitis, in spite of the fact that she has anesthesia of the larynx and cornea. Many girls have that. It may be a neurodermatitis.

Dr. Joseph J. Eller: I agree with those who do not think that this is a case of dermatitis factitia.

Dr. Louis B. Mount: It would be simple to find out if the lesion is self-inflicted. Put on a dressing that cannot be tampered with.

Morphea with Atypical Features. Presented by Dr. Paul Bechet.

J. T., a woman, aged 36, stated that six years previously she had noticed a patch on her right breast, which had gradually extended. A year later, several small lesions appeared on the chest, over both scapulae and on the neck. On inspection she presented a dozen or so small, punctate, white, atrophic spots, some of which were as small as 0.25 mm. in width. On the right breast, the initial plaque showed a few pigmented spots. It was atrophic, and presented the glazed white porcelain color of a patch of old morphea. The peculiar feature of the case was the multitudinous small punctate lesions.

DISCUSSION

Dr. Max Scheer: How would Dr. Bechet differentiate this from lichen sclerosus et atrophicus?

Dr. Paul Bechet: I would not consider the diagnosis of lichen sclerosus. The lesions are perfectly flat, and atrophic in the center, and the typical pearly color of morphea is present. My interpretation of lichen sclerosus is a lesion with a raised sclerosed border with, at times, dark, comedo-like horny plugs, and minute atrophic depressions. None of the lesions, in my opinion, suggests lichen planus sclerosus et atrophicus of Hallopeau or lichen planus morpheicus of Crocker.

Dr. Fred Wise: I agree with the diagnosis of morphea in this patient. The condition belongs to the scleroderma group; it is not true morphea, because of the considerable amount of lichenification in the lesion. It is the type of scleroderma described as lichenoid scleroderma, but the name morphea, I presume, is just as applicable to this lesion as any other.

DR. MAX SCHEER: I think that the condition Dr. Bechet described sounded like lichen atrophicus. I do not think it is possible to make a differential diagnosis.

ALOPECIA AREATA FOLLOWING THALLIUM ACETATE TREATMENT FOR TINEA CAPITIS. Presented by DR. LUDWIG OULMANN.

A girl, aged 8 years, came to the clinic two months prior to presentation. At that time she had numerous crusted lesions with broken-off hairs on the scalp, and received thallium acetate, 8 mg. per kilogram of weight. The scalp was epilated in about four weeks. When the hair returned, she showed an alopecia areata extending throughout the scalp with large patches over the parietal region. Some of the hair had started to return in those spots. The patient also received two ultraviolet light treatments.

DISCUSSION

DR. LUDWIG OULMANN: I regard the condition as alopecia areata due to inflammation combined with a disturbance in certain sectors of the sympathetic nervous system in the cervical plexuses. This inflammation may be caused by metals, by absorption of pus from focal infection, with or without arthritis, or by pressure. When the hair returns, it is a sign that the inflammation is subsiding and the nerves again function. An areated alopecia after the administration of thallium acetate is the same as an alopecia areata developing from other metallic poisoning. In some of the spots the hair is returning and I expect the condition to disappear.

DR. GEORGE C. ANDREWS: I doubt that one should call this alopecia areata. I understand thallium acetate was given two months ago. I do not think, however, that this patient has the disease entity, alopecia areata. The regrowth of hair is occurring in an irregular way.

DR. FRED WISE: I would bring out the point Dr. Andrews spoke of. I do not see on what grounds one could call this alopecia areata. Alopecia areata is an entity, a disease of unknown origin, accompanied by loss of hair, without any known etiologic factors. The patient has loss of hair that looks like alopecia areata, but one cannot prove the diagnosis now; one must wait two or three months.

DR. M. B. PAROUNAGIAN: I think that Dr. Wise's differentiation is a very good one. I am not in favor of using thallium acetate. I would rather let the patient wait several months than take any chance with such a dangerous drug.

HYPERTRICHOSIS OF THE FOREARMS AND LUMBAR REGION IN A GIRL AGED FIVE YEARS. Presented by DR. PAUL BECHET.

G. S., a girl, aged 5 years, presented on both forearms and in the lumbar region an abnormal growth of silky hair, from 2.5 to 5 mm. long, which her mother stated had been present for three years. The skin from which these hairs arose seemed normal, and devoid of the slightest evidence of a nevoid character. She had a well defined Frölich's syndrome.

DISCUSSION

DR. JOSEPH J. ELLER: Has anyone in this society observed the falling out of superfluous hair in later years when the internal glands of secretion functioned normally, following a distinct endocrine disturbance in early youth as shown in this case?

DR. PAUL M. BECHET: I am convinced of the relationship between disturbances of the endocrine glands and hypertrichosis.

In a paper written eighteen years ago, I reported the results of an analysis of 146 cases of hypertrichosis, 106 of the patients being unmarried. In none of the cases did hypertrichosis occur before the establishment of puberty. Of the

106 single women only 4 were less than 18 years of age. Of the 146 patients, 80 had severe menstrual disturbances, but fully 25 per cent of the 65 remaining patients had minor anomalies of menstruation.

In answer to Dr. Eller, I recall that Jackson observed a woman who, after having borne several children, suffered from a persistent amenorrhea during which time extensive hirsuties developed. I reported a similar case recently. Dr. Hyde reported the case of a married woman, aged 33, the mother of three children, who had not menstruated for over a year. She had general and facial hirsuties. After several years she began to menstruate and the hypertrichosis spontaneously disappeared.

KERATOSIS FOLLICULARIS. Presented by DR. PAUL BECHET.

S. C., a woman, aged 28, stated that she first noticed an eruption on her neck about six weeks previous to presentation. It rapidly spread to the trunk, arms and legs. The lesions consisted of greasy-looking, hyperkeratotic elevations, of a reddish-yellow color, and were essentially follicular in appearance. The palms and soles were thickened, keratotic and bright red. None of the lesions was scaly. There were, however, one or two spots on the arms and some in the scalp, suggestive of psoriasis.

DISCUSSION

DR. MAX SCHEER: The presence of scaly patches on and below the knees and in the scalp, the punctate scaly spots and the linear scaly lesions indicate that the patient has follicular and patchy psoriasis.

DR. FRED WISE: I agree with the diagnosis of psoriasis. I think the important point in making the diagnosis in this case is the scratch marks showing bleeding points.

DR. LUDWIG OULMANN: I regard the case as one of keratosis pilaris and psoriasis.

DR. PAUL BECHET: Despite the fact that the lesions on the scalp and knees are psoriatic in appearance, a close inspection will reveal that they are made up of conglomerate patches of exactly the same type of hyperkeratosis as on the rest of the body. According to the history, the lesions have been present for only six weeks. It is rather early to make a diagnosis of Darier's disease, but the lesions are greasy, follicular and hyperkeratotic; I cannot conceive of a psoriasis with this appearance. A point against psoriasis and in favor of Darier's disease is the reddened, thickened keratotic palms and soles, without the slightest scaling.

ACQUIRED PROGRESSIVE KINKING OF THE HAIR OF THE SCALP. Presented by DR. FRED WISE.

This article will be published in full in a later issue of the ARCHIVES.

DISCUSSION

DR. PAUL E. BECHET: I saw this patient on my service at the New York Skin and Cancer Hospital several months before he was seen by Dr. Wise. When I first observed him, only the front third of the hair was involved. The back and sides were normal in color and texture. Since then, it seems that the condition has increased enormously; he has only a few of the original hairs left in front. The increase of the condition has been most rapid. It is an interesting case. The etiologic factors are speculative, and are well worth investigating.

DR. LUDWIG OULMANN: If these changes were caused by chemicals, there would be a clinical or histologic dermatitis present. The changes are due to constitutional causes.

DR. JOSEPH J. ELLER: A case which Dr. Wise presented a few years ago and which was reported in the literature, was that of a child, aged 5 or 6 years,

with a similar condition. The curly condition of the hair did not start until some months after birth. I do not see why this case is not one of delayed hereditary characteristics. Congenital marks, such as nevi, may not appear until many years after birth.

Dr. Fred Wise: The patient works as a drug clerk, but for a long time he has been a student at a night school. He does not handle chemicals. We asked him about the habit of running his hands through his hair. All those points were of no significance. The difference between this case and the one Dr. Eller referred to is that in the latter the mother stated that from birth the hair was curly in a circumscribed area, like an oasis in the desert. The masses of hair around it were normal, straight and slightly darker. In this patient there is no island of hair; the condition is progressive. The disturbance began in front as though following a nerve distribution, gradually progressing from the front toward the side. Of the two children whose cases I previously reported, one was Jewish and one a Gentile Syrian. I bring that point out on account of possible atavism. The Jewish child had curly hair. This patient is also Jewish. Careful questioning about his ancestors brought no light on the matter. Histologic study of the portion of the scalp with kinky hair shows nothing. Careful study of the shaft of the hair does not reveal any change. The hair is thinner in diameter, but there is no sign of dermatitis or nevoid changes in the scalp.

Granuloma Annulare. Presented by Dr. Paul E. Bechet.

A woman, aged 45, stated that lesions had appeared on the back of the neck five years prior to presentation, and had gradually extended to the hands, chest and forehead. On inspection there were violaceous, elevated, serpiginous plaques on the backs of the fingers and hands. On the chest, neck and forehead they were erythematous and comparatively flat. She had markedly improved with the use of a few injections of tuberculin in weak dilution. She reacted strongly to an intracutaneous injection of tuberculin. The Wassermann reaction was negative. A blood count showed: hemoglobin, 100 per cent; red blood cells, 4,360,000; white blood cells, 6,840; polymorphonuclears, 42 per cent; lymphocytes, 56 per cent; mononuclears, 2 per cent; chemical analysis of the blood revealed: uric acid, 3.33; urea, 18.7; sugar, 103, and sodium chloride, 462.

Biopsies were done on lesions on the hand, chest and neck. The sections confirmed the clinical diagnosis. The interesting points in the case were the erythematous lesions on the chest, neck and forehead and the peculiar rapidity of their evolution and involution.

DISCUSSION

Dr. Louis B. Mount: I thought that one lesion on the hand looked like granuloma annulare. I could see no other annular lesions.

Dr. Ludwig Oulmann: I agree with Dr. Mount, that the large lesion with the infiltrated margin is one of granuloma annulare, but I could see nothing in the histologic picture that would speak for that diagnosis.

Dr. Samuel Monash (by invitation): This is one of two similar cases followed at the New York Skin and Cancer Hospital for the past four months. When first observed, this patient had typical lesions of granuloma annulare on the hands, discrete papular or nodular lesions on the chest and back and, in addition, an erythematous area on the left side of the forehead, the last showing practically no infiltration. Biopsies were performed on all of the aforementioned areas. All of them, including the erythematous area on the forehead, showed similar microscopic pictures. The lesions were mainly in the dermis, consisting essentially of an infiltration of epithelioid cells with a few giant cells and areas of necrosis in some of the sections. She had been previously treated at the Post-Graduate Hospital where Dr. Satenstein had made a diagnosis of granuloma annulare on the sections prepared there. She gave a strongly positive reaction to an intracutaneous injection of old tuberculin, 1:1,000; in addition, a subcutaneous

injection of 0.001 mg. of old tuberculin resulted in definite infiltration in the dermis. The results of the inoculation of guinea-pigs were negative.

DR. PAUL BECHET: She has two types of lesions: typical nodular annular, violaceous lesions on the hands and wrists, with depressed centers, and peculiar erythematous lesions on the forehead, neck and chest. A point against tuberculosis is the ephemeral character of the lesions. They show a tendency to disappear with almost no treatment. I favor the diagnosis of granuloma annulare rather than tuberculosis.

LUPUS VULGARIS. Presented by DR. LUDWIG OULMANN.

A woman, aged 45, had been operated on for enlarged glands of the neck at the age of 19. At that time she had a few red nodules of lupus vulgaris on the cheek and neck. They spread over both lower cheeks and around the neck to the angles of the maxillae. The patient had had many kinds of treatment for the nine years prior to presentation, including numerous roentgen treatments. When she came under my care in March, 1930, I started to treat her by inserting toothpicks dipped in 50 per cent phenol and alcohol into each nodule, putting her on a salt-free diet and prescribing cod liver oil. From June to October the patient had no treatment, and since October she had had five treatments. She was presented to show the good results achieved in so short a time.

DISCUSSION

DR. FRED WISE: I think the result is excellent for lupus vulgaris, which is difficult to treat. The interesting thing in this patient is how much contracture one is liable to produce in a scar after treatment with phenol punctures. The idea I have in mind is that contractures on the face and neck would probably be greater than that from the orthodox treatment by Finsen light, of which so many examples are seen in Europe. On account of the flaccidity of the skin in this patient, I think the final result will be good.

DR. H. J. F. WALLHAUSER: I agree with Dr. Wise regarding the good results obtained with Finsen's light at Copenhagen. The results there seem to be very much better, especially in the cosmetic effects, than with any other treatment employed in this country. However, the case presented by Dr. Oulmann tonight shows remarkable improvement and should progress favorably with the method employed.

DR. MAX SCHEER: The result that Dr. Oulmann has shown seems good, but I am skeptical as to the ultimate result. I have seen patients treated with phenol and with trichloracetic acid and usually new nodules appeared, very often in the scars of the old lesions. The time to judge the result in cases of this kind is after a year or two.

DR. M. B. PAROUNAGIAN: The results seem to be very good, but I must say I have had some very excellent results from injections of a gold compound in some cases of lupus vulgaris.

DR. GEORGE C. ANDREWS: Dr. Edgar Mayer, of Saranac Lake, visited Sauerbruch's clinic in Munich and Jesionek's clinic in Giessen, under the auspices of Mr. August Heckscher, to observe the results being obtained by diet in tuberculosis. The most benefit was observed in lupus. The diet is low in sodium chloride, protein and carbohydrate content but rich in fats and vitamins. Dr. Mayer concluded that the organic constituents, whether acid-forming or base-forming, were not as important as the vitamin content.

LICHEN PILARIS SPINULOSUS. Presented by DR. PAUL E. BECHET.

J. W., a man, aged 22, first noticed the eruption on his neck. Within a short time it spread to his arms and body. He presented the typical grouped, spiny, epidermic pegs in the center of a conical papule.

PEMPHIGUS. Presented by DR. PAUL E. BECHET.

J. G., a man, aged 75, a Jew, presented on examination a dried, crusted eruption on the scalp and bullae on the hard and soft palate. The lesions had begun on the scalp four months previously, and a month later also appeared in the mouth. There was also a superficial crusted lesion on the nose. His general health was fair, and he had not lost any weight. Dr. Pels reported a toxic reading of 58 per cent on the Macht-Pels test.

BLASTOMYCOSIS. Presented by DR. GEORGE C. ANDREWS.

B. G., a man, aged 30, had been sick for three years with an eruption that had begun on his cheeks. At the time of onset, he was not in contact with cattle, animals or animal products. Five years previously he had handled hides. He believes that the infection was acquired in a barber shop. Blastomyces were demonstrated in the pus from the lesions on the cheeks, and they were cured by iodides and roentgen treatment. However, extensive patches had developed on the lower part of the buttocks, and in a collar-like band about the neck. These were present at the time of presentation, together with the scars of the previous lesions on the face. The areas were now being treated with x-rays, and the patient was receiving maximum doses of iodides intravenously and by inhalations, as his stomach would not tolerate iodides.

MOTTLED CHIN DUE TO SYPHILIS. Presented by DR. M. B. PAROUNAGIAN.

I. D., a woman, aged 24, had been seen at the Bellevue Hospital on Jan. 6, 1931, for the first time. Her history was vague, and she was ignorant of her condition. However, examination readily disclosed the diagnosis of secondary syphilis, as she had condylomas about the genito-anal region, marked adenopathy and a deeply pigmented eruption about the mouth and chin with occasional circinate papules. Her Wassermann reaction was four plus. The pigmentation on the chin and about the mouth was unusually pronounced.

ST. LOUIS DERMATOLOGICAL SOCIETY

MARTIN F. ENGMAN, JR., M.D., *Secretary*

Regular Meeting, Jan. 14, 1931

RICHARD S. WEISS, M.D., *Presiding*

ERYTHRODERMIE PITYRIASIQUE ET PLAQUES DISSÉMINÉES, BROCQ. Presented by DR. A. H. CONRAD.

F. L., a white man, aged 31, an inspector, presented himself on May 7, 1930, with the complaint of a rash on his body of three months' duration. Examination at this time showed lesions of from ½ to 2 inches (1.27 to 5 cm.) in diameter, scattered over the trunk and the upper part of the thighs.

The eruption was characterized by scaly, elevated plaques some of which were quite sharply defined and some of which coalesced to form the larger plaques. They were pale red, and the surface was covered with a very profuse light scale.

At this time he gave a history of a "mother patch," and a diagnosis of pityriasis rosea was made. I saw him only three times from May 7 until May 17, when he left town, his condition being somewhat improved by the use of the ultraviolet rays.

I did not see the patient again until Jan. 2, 1931. Examination on this date showed the same lesions, but they were much more profuse, especially on the thighs and the back. He complained of much itching, especially on the back.

DISCUSSION

DR. JOSEPH GRINDON: I think that this case is one of the third of Brocq's three types of parapsoriasis; what might be called the pityriasis rosea-like type; that is, it is the type named by Dr. Conrad.

DR. R. S. WEISS: I agree with Dr. Grindon in the diagnosis of erythrodermie pityriasique en plaques disséminées.

TULAREMIA, ULCEROGLANDULAR TYPE. Presented by DR. W. G. COLEMAN.

Mrs. O. W., a woman, aged 54, said that she had become ill with a chill, headache, burning of the eyes and severe articular and muscular pains, followed by fever of 103.5 F. for a week, after which it was intermittent.

On Dec. 13, 1930, a shallow ulcer one-half inch (1.27 cm.) in diameter had formed over the medial end of the left radius. The base consisted of granulation tissue; the border was grayish, rolled and indurated, and it was surrounded by an erythematous border three-fourths inch (1.87 cm.) in diameter. The ulcer had a punched-out appearance. There was no pain and little tenderness. The axillary glands were palpable.

At present there is a crusted ulcer on the left wrist with a pinkish areola about one-half inch in diameter. The axillary glands are still firm, and they form a mass about 2½ inches (6.27 cm.) in diameter.

The patient had prepared rabbits about one week before the onset of the illness.

The blood serum gave a positive agglutination for *Bacillus tularense* in a dilution of 1:60, at the National Institute of Health, Washington, D. C., but the routine test for undulant fever gave negative results.

DISCUSSION

DR. JOSEPH GRINDON: Was there a rise in temperature?

DR. W. G. COLEMAN: The peak was 103.5 F.

DR. JOSEPH GRINDON: Was the patient very ill?

DR. W. G. COLEMAN: Yes, she had severe headaches, malaise and other disorders.

DR. JOSEPH GRINDON: To the best of my knowledge, the disease has been found only in wild rabbits and not in domestic ones.

DR. E. C. BROCKELMANN: In this connection I wish to mention a case I brought up here some time ago. The patient, who was employed at a meat market, where from 200 to 300 dozen rabbits were graded and skinned daily during the season, had a positive history of tularemia infection, but repeated serologic tests over a period of several months failed to give a positive agglutination for *Bacillus tularense*.

The patient had ulcers of the type seen in ulceroglandular tularemia, but they were multiple on both hands, and slowly healing, and they kept on forming continually. At that time no one here seemed to be willing to express an opinion as to the nature of these ulcers, and the diagnosis of tularemia was doubted. Following this I made investigations at the meat market and found that three other men who did the same work were infected at about the same time. Serum from each one of these men strongly agglutinated for *Bacillus tularense*, and one of the men also showed continuous ulcer formations.

I wrote to Dr. Edward Francis in Washington, D. C., about the cases, and sent him serum on request. In his reply, however, he did not want to venture an opinion.

Only these two of about a dozen cases of tularemia seen by me showed such atypical features.

As four varieties and many complications due to *Bacillus tularense*, like appendicitis, pleuritis, pneumonia, etc., are known so far, it is worth while, I find, to look out for other atypical forms.

The patient mentioned had a recurrence of ulcer formation one week ago (i. e., fifteen months after infection), after having been free from symptoms for more than six months.

A CASE FOR DIAGNOSIS. Presented by DR. W. G. COLEMAN.

Miss E. M., aged 30, had had the usual diseases of childhood, and influenza in 1928. The present illness had begun two years before examination, when the patient noticed that her finger-nails were more brittle and had a tendency to turn back from the nail bed.

In June, 1930, while she was on a train from St. Louis to Los Angeles, the fingers to the second joint became swollen and painful, followed by a vesiculopapular eruption. There were no lesions on the feet. At this time there was a similar eruption under the nails. The cutaneous eruption was treated with three per cent boric acid in petrolatum, and it disappeared in about two weeks. There had been a series of eruptions under the nails, and the nails had "grown away from the fingers."

At present, a vesiculopapular eruption can be seen through the nails, which are undermined for about one third of their length.

DISCUSSION

DR. R. S. WEISS: I would examine scrapings from underneath the nails for dermatophytes. Another diagnosis I would consider is acrodermatitis chronica perstans.

DR. M. F. ENGMAN, JR.: Recently there was an article in a British journal to which Dr. Weiss and I were attracted, and in which Barber classified some of these cases as psoriasis of a pustular form.

DR. N. W. SCHLUETER: I suggest a diagnosis of onychomycosis.

A CASE FOR DIAGNOSIS. Presented by DR. RICHARD S. WEISS.

A white man, aged 37, entered the clinic of Dr. Engman and Dr. Mook, at the Washington University Dispensary, on Dec. 16, 1930. His family history was irrelevant. The important points in the past history were pneumonia at the age of 18, which was followed by pulmonary tuberculosis. He was treated by Dr. Albert Taussig, pneumothorax treatment being used. He was discharged as cured.

The present illness began about ten weeks ago with a blister on the middle of the right leg. This ruptured and an ulcer appeared and spread fairly rapidly. He had had many and various treatments.

Examination disclosed a large ulceration on the middle third of the right leg, about 6 by 4 inches (15.24 by 10.16 cm.) in size. The surface was in part verrucose and in part oozing ulceration. The borders were serpiginous and slightly elevated and rolled, and the center showed a tendency toward healing.

Examinations for blastomycetes and other fungi were negative in smear and culture. Examination for ameba gave negative results.

The reactions to the Wassermann and Kahn tests were negative on entry. The patient was given 0.3, 0.45 and 0.45 Gm. of neoarsphenamine, and the reactions to the Wassermann and Kahn tests were negative after each dose. No improvement resulted from this treatment.

DISCUSSION

DR. JOSEPH GRINDON: This case looks very much like one of bromide dermatitis. It might be an unusual type of tuberculous lesion

DR. E. R. BROWN: Is there not a possibility that this patient has tuberculosis and that he has taken bromides?

DR. R. S. WEISS: I think that Dr. Brown's suggestion of a bromide eruption as the primary condition is very good. I confess that I did not think of bromides. We will have a specimen taken for biopsy, and make a careful study of it.

A Case for Diagnosis. Presented by Dr. Henry C. Shaw.

L. C., a colored girl, aged 3 years, was seen at the Barnard Free Skin and Cancer Hospital, on the service of Dr. Engman and Dr. Mook. The mother was under treatment for syphilis, which was probably contracted one year after the birth of this child.

The child, while appearing well nourished, had always been in rather poor health.

The present illness began about six months ago as a papule on the back of the neck, which ulcerated and spread slowly to its present size. There had been no constitutional symptoms since the onset.

Examination showed a well nourished colored child, who appeared and acted chronically ill. There was an indurated, dirty granular ulcer on the back of the neck, 2 cm. in diameter. The glands in the anterior cervical chains were enlarged and firm.

The Wassermann and Kahn reactions of the blood were negative. The cytology of the blood was normal. Roentgen examination of the chest showed the following changes: "The hilar and peribronchial structures indicate semi-active infiltrations. These findings are somewhat suggestive of tuberculous pathology."

Results of biopsy were not reported.

The patient had been under observation in the clinic for one month. She had been placed on a high caloric and high vitamin diet and had been placed under the care of the Municipal Visiting Nurses. The ulcer had shown some improvement. (Six per cent xeroform was administered locally.)

DISCUSSION

Dr. Joseph Grindon: I think that it is a tuberculous condition; however, while tuberculous lesions usually have a soft border, the border of the ulcer presented is hard. While a malignant condition may exist in early childhood, we all know that it is rare to find carcinoma in young children.

Dr. A. H. Conrad: We thought that it was a tuberculous condition of the skin, though it has cleared up very much since the patient came in. The condition has been present for two and a half years, and in the short time the patient has been under treatment, it has cleared up remarkably well.

I wish to add that a roentgenogram showed involvement of the lungs. A report of the biopsy has not yet been made.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Jan. 21, 1931

Clark W. Finnerud, M.D., *President, Presiding*

Perlèche, Erosio Interdigitalis (Hands), Chronic Intertriginous Mycotic Dermatitis (Feet, Groins and Inframammary Region) and Mycotic Vulvitis and Vaginitis. Dr. Clark W. Finnerud.

A woman, aged 64, presented an erythematous, scaling dermatitis of the inguinal regions and groins of twenty years' duration. A similar eruption had appeared beneath the breasts within the year prior to presentation. She stated that for twenty-one years she had had involvement of the interspaces of the fingers and for a lesser time between the toes. The involvement at the angle of the mouth had been periodic, but it had extended over a considerable number of years. Irritation had been present in the region of the vulva and vagina, sometimes particularly noticeable on urination, for many years.

Cultures were made of scrapings from all areas, and colonies of yeast that proved microscopically to be devoid of mycelium made their appearance on maltose-agar medium on the second and third days. Morphologically, the organism was *Cryptococcus,* the same organism being obtained from all areas.

DISCUSSION

DR. H. M. HEDGE: Is there any theory as to the reason for the particular location of these lesions between the ring and middle fingers?

DR. J. H. MITCHELL: The only explanation I have to offer is that in ordinary movements of the fingers there is more or less constant approximation of the third and fourth fingers, whereas the second and fifth are separated from the adjoining members. Moreover, in the obese patient—who seems to be the victim of this disorder—there is complete apposition of the surfaces of the proximal phalanges of the third and fourth fingers, thereby forming perfect conditions for the growth of *Monilia.*

DR. CLARK W. FINNERUD: I think that Dr. Mitchell's statement explains the location of these lesions on both the feet and the hands.

ROENTGEN DERMATITIS. DR. W. W. DUELMING.

C. R., a man, aged 35, was first seen about one month prior to presentation because of an eruption that involved the dorsal areas of both hands and the extensor surfaces of the arms. His past history was irrelevant, except that twelve years before he began receiving roentgen therapy for an eruption on the backs of his hands. This treatment was continued without interruption for seven years, but the number of treatments per year and the dosage could not be accurately ascertained. In 1927, an ulcer developed on the dorsum of the right hand and had persisted since that time. During the year and one-half before presentation, the patient spent fourteen months at the Great Lakes Naval Hospital, and during that time the ulcer decreased slightly in size. Extreme pain had been a periodic and distressing feature of the case.

The eruption involved the backs of the hands and fingers and the extensor surfaces of the forearms, almost to the elbows. In the areas in which the skin had not broken down, there was mottled brownish hyperpigmentation and depigmentation, together with marked telangiectasia, atrophy and loss of the normal markings of the skin. Several hyperkeratoses were present, varying in size from that of a glass pinhead to that of a large bean. The nails presented marked ridging, which is evidence of nutritional change. An ulcer, roughly U-shaped, occupied half the surface of the back of the right hand. The base was made up of infected granulation tissue, and for the most part, the border was covered with a hyperkeratotic crust. The patient was unable to flex the fingers of the right hand, except very slightly. The left hand presented practically the same changes, except that, over the back of this hand, instead of the ulcer, there was a larger hyperkeratotic crust, which had been partially removed by treatment. To palpation, the involved areas had an almost boardlike hardness.

DISCUSSION

DR. UDO J. WILE: Cases of roentgen dermatitis as destructive as this that I have seen have yielded only to grafting, and I should suggest that procedure in this case.

DR. H. E. MICHELSON: In a roentgen ulcer one must first be sure that the limits of the destruction have been reached. We have found that complete débridement with a cautery usually gives a clean granulating wound. On the hands, we have found that the insert grafts leave a very thick pad and are therefore objectionable. Dr. Rusten of our clinic does a clever implant graft. He uses an intestinal needle, and with this he buries minute Thiersch grafts deep in the granulating

tissue. It is amazing to see the growth from these little islands of epidermis come to the surface and spread across the area. The granulating tissue shrinks away, and the result is very satisfactory.

DR. OLIVER S. ORMSBY: I have seen a case after the operation described by Dr. Wile has been performed, and I have seen the puffiness removed by a second operation, with good results. In most cases of ulcers on the back of the hand, the great problem is to save the tendons. If an operation can be performed without interfering with the tendons, it is successful; otherwise, it is a failure.

DR. W. W. DUEMLING: The point that Dr. Ormsby brought up regarding involvement of the tendons is of considerable importance in this case. The patient has a claw-hand and is not able to flex his fingers to any degree, showing that the tendons have been involved. This deformity, however, may be due in part to the fact that the hand was immobilized in a splint while the patient was under treatment at the Great Lakes Naval Hospital.

LUPUS ERYTHEMATOSUS. DR. F. E. SENEAR.

Mrs. M., aged 32, was first seen in August, 1925, because of typical lupus erythematosus of the face. The condition had been present for several years, and considerable scarring had resulted. The patient was treated with carbon dioxide snow, and apparently made a good recovery.

She returned in November, 1930, at which time the scarred areas showed a large number of brownish-red infiltrated papules and plaques, which had appeared three months before.

DISCUSSION

DR. O. H. FOERSTER: I think that the condition is a recurrence of lupus erythematosus rather than recently developed lupus vulgaris. The clinical picture is influenced by the extensive destructive changes that have occurred in the skin, as shown by the atrophic scarring around the margin of the lesion. I could not convince myself of the presence of lupus nodules. The vascular element is pronounced, and my impression is that it is lupus erythematosis.

DR. F. E. SENEAR: This patient was presented with the idea that the present condition might be lupus vulgaris. I discussed the case with Dr. Foerster when we saw the patient together this afternoon, but I am not convinced that anything except a biopsy will show the real nature of it. The fact that new lesions begin as pinpoint-sized, slightly elevated papules and new patches form by coalescence, with no primary lesions, impressed me that the condition was possibly lupus vulgaris. I do not think that there is any sharply defined apple jelly nodulation, but more is present than would be seen in lupus erythematosus, although I recognized, as Dr. Foerster pointed out, that the condition is remarkably telangiectatic.

LUPUS VULGARIS (TREATED BY THE GERSON DIET). LUPUS ERYTHEMATOSUS? DR. CLEVELAND J. WHITE.

A woman, aged 55, presented an eruption on her face which had been present for eight years. She had received various forms of treatment, including the administration of carbon dioxide snow. She was told to eliminate salt and carbohydrates from her diet as far as possible, and to eat eggs, tomatoes, oranges, spinach and other green vegetables and fruits, and to drink milk. She was also given cod liver oil. Two weeks after beginning this regimen she was much better, and her condition had improved rapidly for two months.

DISCUSSION

DR. UDO J. WILE: The case appeared to me to be lupus erythematosus rather than lupus vulgaris. In cases of lupus vulgaris in which the salt-free diet has

been used, the result, or improvement, has been extraordinarily slow. It takes place only after several months.

DR. H. E. MICHELSON: I agree with Dr. Wile that, morphologically, the lesions on the skin are lupus erythematosus, but the patient's history and scars are those of cervical adenitis, and she stated that these glands have suppurated for years. It would be advisable to perform a biopsy; we may be dealing with a case of lupus erythematosus in a tuberculous person.

The Gerson diet is not easy to carry out, and cannot be ordered from most diet kitchens without special instruction.

DR. A. W. STILLIANS: I am sorry that we did not have better proof of the diagnosis in this case. I asked the patient how she made the diet palatable, and she told me that she used spices, garlic, and so on. She is intelligent, and I think got along better than many persons would. She is still on the diet.

LUPUS VULGARIS, HYDROCYSTOMA AND MULTIPLE FIBROMAS. DR. CLARK W. FINNERUD.

A housewife, aged 52, presented herself because of three lesions of the medial surface of the skin of the right leg which had been present for thirty-six years. She stated that she had injured this leg a few years before the appearance of the lesions, and that an operation had been performed for the injury. The lesions had appeared about two years after the operation, and had gradually developed to their present size.

The three lesions on the leg and the thigh were slightly elevated, reddish-brown, soft plaques, the size of a large coin and larger; on pressure with the diascope, distinct brownish nodules were evident. Two of the lesions had cleared centrally, leaving atrophic scarring. In the lower half of the leg there was marked deformity, the result of the injury and the subsequent surgical operation.

The patient also presented numerous, slightly bluish-white nodules, the size of a pinhead and larger, on the face and the forehead. On puncture, the nodules were found to be filled with a clear fluid. She also had numerous filiform fibromas of the face and neck.

DISCUSSION

DR. CLARK W. FINNERUD: I should like to know whether anyone thinks that the condition is sarcoid rather than lupus vulgaris.

DR. H. E. MICHELSON: I think that multiple acupuncture with a cautery of the Cameron type gives good results in selected cases of lupus vulgaris.

DR. DAVID LIEBERTHAL: This is the first case of this type that I have seen demonstrated before this Society. These cases are more frequently seen in European clinics.

DR. F. E. SENEAR: I was interested in this case in a general way because we teach that lupus vulgaris is a disease occurring in young persons, chiefly on the face. It so happens that the last five cases that we have had at the University of Illinois have been in adults; they have often started in early life, and in none has the face been involved. It is rather embarrassing to teach students one thing, and then to present patients who do not fit in with the teaching.

DR. RUBEN NOMLAND: At the dispensary, we probably see three or four cases of hydrocystoma and about the same number of cases of lupus vulgaris in a year. This case is interesting because the two conditions are present in the same patient.

DR. CLARK F. FINNERUD: I understand that this patient has not received treatment. Any improvement that has occurred has been spontaneous, and some of the lesions have undergone partial involution.

PARAPSORIASIS WITH PALMAR LESIONS. DR. W. A. PUSEY and DR. L. F. WEBER.

A white woman, aged 28, stated that three years before presentation a generalized eruption had developed which was diagnosed as syphilis on a doubtfully positive Wassermann reaction. Treatment with neoarsphenamine was started, but before the course was completed, dermatitis exfoliativa developed, which confined the patient to the hospital for nine weeks. After she had left the hospital, the condition of the skin showed considerable improvement, and the Wassermann reaction was reported negative. Four months later the eruption reappeared on the extensor surfaces of the forearms, it gradually became generalized. There are lesions on the palms. She came under our observation after the second attack had been present for three months.

PARAPSORIASIS. DR. M. R. CARO for DR. E. P. ZEISLER.

A white man, aged 41, stated that the eruption had been present for about five years and that it had been generalized from the onset. It had remained practically unchanged and was unaccompanied by pruritis or other symptoms.

The eruption was generalized and consisted of ill defined, pea-sized, pinkish-red, erythematosquamous lesions, covered by thin, dry scales. No lesions were present on the palms or soles, and there were no areas of leukoderma.

DISCUSSION

DR. UDO J. WILE: Has anyone besides myself been impressed by the occurrence of lesions on the palms? I have never seen this location involved before, and it seems to me very unusual.

DR. O. H. FOERSTER: I recently saw this rare involvement in a man who had lesions on the palms but not on the soles. Leukoderma is frequently associated with this disorder, perhaps more often than with any other dermatosis. Neither of these patients, however, had leukoderma.

DR. OLIVER S. ORMSBY: It seems that this particular type of parapsoriasis is the most common. We probably see six or eight of these cases to one of the other type. Involvement of the palms is rare; this is the first case that I have ever seen.

DR. CLARK W. FINNERUD: I think that I saw parapsoriasis with lesions on the palms, punctate keratoses, in a patient of Dr. Oppenheim's.

DR. L. F. WEBER: So far, I have found only two references in regard to lesions on the palms and soles.

XANTHELASMA (UNUSUAL DISTRIBUTION). DR. E. B. RITCHIE (by invitation).

A woman, aged 52, complained of abdominal distress, jaundice, pruritus and loss of weight that had been present for from six to eight months. Study revealed cirrhosis of the liver with jaundice and a duodenal ulcer that produced obstruction. An accurate history could not be obtained regarding the duration of the lesions about the eyes and on the neck, or their association with her general condition.

In addition to a moderate degree of jaundice, examination revealed elevated yellow plaques over the inner half of both upper and lower lids and in the region of the inner canthi. On the neck, extending to the sternum and back almost to the nuchal region on both sides of the neck, were fairly well defined, mottled, yellow, elevated patches.

A specimen was removed from the left side of the neck for biopsy. Sections stained for fat showed marked deposits of fat in the upper part of the corium, just below the epidermis, and large globules of neutral fat deep in the corium about the sweat glands.

DISCUSSION

DR. UDO J. WILE: I agree with the diagnosis. The lesions on the neck were striate and suggested to Dr. Michelson and myself that they might possibly be lesions of myeloid degeneration, but under the microscope they were seen to be full of fat, which is at least presumptive evidence that they are due to deposits of fat. The association of cirrhosis of the liver has been noted before. A disturbance of the liver is closely associated with fat metabolism, which explains the appearance of vicarious fat in the skin.

DYSKERATOSIS (BOWEN). DR. A. W. STILLIANS.

A man, aged 63, an American, first noticed a red patch on the right buttock in the fall of 1929. It had not caused discomfort until about a month before presentation, and it had been slowly increasing in size.

There was a yellowish-red, round patch of thin skin, about 3.5 cm. in diameter, on the upper part of the right buttock. In the center was a large flaccid bulla. The border was sharply defined but not elevated. There was no infiltration.

Biopsy showed acanthosis and pyknosis of the epithelial cells at the border of the specimen, a heavy granular layer and a spongy looking horny layer. There was marked edema of the upper cutis in some places about the blood vessels, and a slight infiltrate. At the center of the patch the basal and prickle cells were not seen, only balloon cells with pyknotic nuclei. The blood vessels of the upper cutis were dilated, and there was marked edema in places.

DISCUSSION

DR. J. H. MITCHELL: Was a sinus present?

DR. A. W. STILLIANS: No.

DR. DAVID LIEBERTHAL: What did the urine show?

DR. A. W. STILLIANS: Urinalysis gave negative results, and there was no history of medication. The condition has been constant for years; we thought that it was beginning Bowen's dyskeratosis.

DR. RUBEN NOMLAND: Is it possible that this condition might be akin to match-box dermatitis?

DR. O. H. FOERSTER: I had thought of that possibility too, but dismissed it because of the lack of corroborating history and essential clinical features.

ANNULAR PAPULAR SYPHILIS (OCCURRING ALMOST SIMULTANEOUSLY IN A FATHER AND THREE YOUNG CHILDREN, THE ERUPTION LIMITED TO THE FACE AND NECK AND IN EACH INSTANCE WITHOUT HISTORY OR EVIDENCE OF A PRIMARY LESION). DR. CLARK W. FINNERUD.

A colored man, aged 30, was first seen about one month before presentation with a classic annular papular secondary eruption of syphilis, limited to the face and neck, of one and one-half months' duration. He also presented general superficial lymphadenopathy, condylomas about the anus and a strongly positive Wassermann reaction. He brought with him to the clinic his 10 year old son, who had practically an identical eruption of six weeks' duration, but no condylomas. However, he did have general lymphadenopathy and a 4+ Wassermann reaction. Like his father, he did not give a history of a primary lesion, nor was any evidence of one disclosed on thorough examination. His eruption, like that of his father, had practically cleared in the past four weeks of treatment, the outline of the lesions existing merely as hyperpigmentation.

The wife and mother was said to have had identical symptoms four months previous to the time of the appearance of the eruption in the father. Her eruption entirely cleared under antisyphilitic treatment, which she was still receiving. Within the week prior to presentation, another child, aged 4, and still another, aged 2, had presented themselves with an identical circinate eruption limited to the

face and neck; they did not give a history of a primary lesion, and on examination no evidence of one was found. The 2 year old child, like his father, had condylomas about the anus. The Wassermann reaction of these children was also 4+.

Laboratory examination of scrapings from the lesions of two of the children did not disclose fungi.

DISCUSSION

DR. OLIVER S. ORMSBY: This is an extraordinary presentation; I cannot account for the occurrence.

DR. J. H. MITCHELL: Is it possible that the condition might be yaws?

DR. OLIVER S. ORMSBY: The history is that of yaws, but the lesions are not. The patients come from a part of the country in which yaws is possible but not probable.

DR. CLARK W. FINNERUD: In the patients presented, the lesions have cleared except for hyperpigmented relics that outline some of the former lesions. The other patients were not able to be presented because of an infection of the respiratory tract with high fever.

DR. F. E. SENEAR: We had a somewhat similar experience about a year ago, in which the first patient presented was a defective boy, aged 14. He exhibited a chancroid about the anus, and we thought that primarily it had probably been an anal chancroid. Three or four other patients were presented, each with a similar eruption but no further evidence of syphilis. Each case yielded spirochetes and a positive Wassermann reaction, but there was no evidence other than the secondary lesions.

A CASE FOR DIAGNOSIS (PERNIO?). DR. A. W. STILLIANS.

An American boy, aged 19, complained of "lumps" on his fingers, which had been present for the past two or three months, and of a few on his feet, which had been present for six or seven weeks. He experienced much discomfort from the deformity of the fingers.

Examination showed many deep, doughy, subcutaneous masses on the fingers and a few superficial, round, doughy, flat-topped, purplish nodes principally on the palmar surface. The lesions on the feet were small, ill defined patches. In the right axilla, the glands were hard and enlarged, but they were not tender or confluent. Both epitrochlear glands were palpable. The other glands were not abnormal.

The results of the Wassermann and Kahn tests were negative. Examination of the blood showed 4,850,000 red cells and 7,800 white cells; the differential count revealed: polymorphonuclear neutrophils, 56 per cent; small lymphocytes, 29 per cent; large lymphocytes, 8 per cent; eosinophils, 3 per cent; basophils, 1 per cent, and transitionals, 2 per cent.

DISCUSSION

DR. LESTER WIEDER: The patient complains of spasmodic pain in the extremities. He has a very slow pulse, and I think that a neurologic examination should be made to rule out a lesion of the central nervous system, possibly a syringomyelia, or a similar process affecting the vasomotor centers.

DR. H. M. HEDGE: I also thought of a lesion of the central nervous system, because the patient gave a history of having taken medicine on several occasions during the past years. He also gave a history of "jerky spells" that were very troublesome, associated with systemic upset.

DR. H. E. MICHELSON: I think that this is a case of chilblain lupus of the Hutchinson type, and I believe that there is a distinct occupational connection. I have seen similar cases in grocers and butchers, and I have noticed that when they cut their hands, especially over the knuckles, the cut becomes infiltrated and remains as a painful fissure for a long while.

DR. LESTER WIEDER: On this basis, how would Dr. Michelson account for the lesions on the feet?

DR. H. E. MICHELSON: I asked the patient about those lesions, and he said that he worked in a grocery store where the floors are very cold. He also stated that his trouble was present only in the winter.

DR. RUBEN NOMLAND: The patient also has a painful nodule in the ear, which speaks for a circulatory disturbance.

DR. A. W. STILLIANS: I was undecided between the diagnosis of pernio and sarcoid, because of the superficial lesions that were present at my first examination, but are absent today. The lesions on the feet did not amount to anything, as long as I observed them.

MINNESOTA DERMATOLOGICAL SOCIETY

Feb. 4, 1931

C. A. BOREEN, M.D., *President, Presiding*

PAPULAR SYPHILIDS RESEMBLING LICHEN PLANUS. Presented by DR. L. H. WINER, Minneapolis.

M. H., a white woman, aged 19, from Dr. S. E. Sweitzer's Service at General Hospital, presented an eruption on the arms and the thighs. She had a macular eruption on the chest and the arms in December, 1930, which remained for two weeks. About Jan. 1, 1931, she noticed a new eruption on the forearms and the thighs.

Examination showed a fading macular eruption that was especially evident on the forearms and, associated with papular lesions, was most marked in the antecubital fossa and on the flexor surface near the wrists. Over the areas where the lesions were most numerous, the arrangement was annular. Similar lesions had been present on the medial surfaces of the thighs and in the intergluteal fold.

The Wassermann reaction of the blood was positive, and the Kahn reaction was 4+. Biopsy showed papular syphilis.

PITYRIASIS LICHENOIDES CHRONICA. Presented by DR. H. E. MICHELSON, Minneapolis.

A woman, aged 22, had a generalized squamopapular eruption extending from the neck to the heels for four months previous to presentation. Of particular interest was the fact that the eruption was present on the soles and the palms. The papules were round or oval and brownish and bore a thin scale that was removed with difficulty. The Wassermann reaction gave negative results. Treatment consisted of irradiation with ultraviolet light, which brought about some involution.

DISCUSSION

DR. F. R. WRIGHT, Minneapolis: I believe that there was a history that this patient had been treated with bismuth for a long time. There are certain syphilitic lesions that bismuth does not affect. I am treating a boy at the present time, and I can feed him bismuth continually without affecting the lesions. He has late secondary or cutaneous gummas. Mercury or arsphenamine clears up the condition immediately, but bismuth does not affect it.

A CASE FOR DIAGNOSIS. Presented by DR. J. F. MADDEN, St. Paul, for DR. H. E. MICHELSON.

H. J., a woman, aged 18, first noticed an eruption on the neck, shoulders and flanks a year before presentation. It consisted of discrete, inflammatory,

lichenoid papules, the size of pinheads, grouped in irregular patches that varied in size from that of a dime to that of a silver dollar. A diagnosis of lichen chronicus simplex was made at that time. The eruption disappeared under local treatment and roentgen therapy, only to recur three months later. The patient was again treated in the same manner, and the eruption disappeared a second time. This was the third recurrence and, in addition to the condition previously described, there was a weeping, inflammatory, crusted eruption on the face and scalp.

DISCUSSION

DR. L. A. BRUNSTING, Rochester: There were certain areas of acute dermatitis about the forehead and the ears that were suggestive of dermatitis venenata, and the patient admitted that she had applied a proprietary ointment to the scalp on several occasions. The lesions over the cubital and supraclavicular fossae simulated lichen planus, but were probably the scratch papules of lichen simplex chronicus.

DR. J. F. MADDEN, St. Paul: We thought of the possibility that the patient had applied some external remedy to the areas in the scalp and the temples, which probably produced a second eruption entirely different from the original one. I think that there is a dermatitis venenata superimposed on some other eruption, probably lichen chronicus simplex.

DR. H. E. MICHELSON, Minneapolis: Our impression is that this is a case of lichen chronicus simplex of the papular type. I like to divide these conditions into two types, the plaque type and the distinct papular type, although at times both elements are present in the same case.

DR. C. E. BOREEN, Minneapolis: I never saw a case of lichen simplex with that distribution.

DR. S. E. SWEITZER, Minneapolis: I think that one could probably rule out a diagnosis of lichen planus in this case and call the condition lichenification. The patient certainly has definite lichenification, and she gets it in certain areas that are usually involved in a chronic dermatitis. If one considers lichen simplex as occurring only in plaques, one could call this a lichenification of a chronic dermatitis.

LICHEN PLANUS, FOLLOWING A DIAGNOSIS OF PITYRIASIS ROSEA. Presented by DR. F. W. LYNCH, Minneapolis.

I. G., a white man, aged 42, from Dr. S. E. Sweitzer's Service at General Hospital, presented an eruption confined to the trunk and the thighs. On Dec. 20, 1930, he presented himself at the Minneapolis General Hospital showing an inflammatory, generalized eruption composed of scaling papular lesions varying in size from that of a match-head to that of a bean, and confined to the trunk and the lower extremities. He had experienced little or no itching. A diagnosis of pityriasis rosea was made, and the eruption was treated with a mild ointment. Early in January, the eruption changed; it became more discrete and was composed of irregular papular lesions, the size of a match-head. The tops of the lesions were smooth and they were of a darker hue. Biopsy was done on Jan. 17, 1931, and showed a definite lichen planus.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I might add that recently we have made observations on two of these patients who when first seen by us, presented a condition that resembled pityriasis rosea. In a week they showed definite signs of lichen planus, and biopsy established the diagnosis.

A CASE FOR DIAGNOSIS (ERUPTION CAUSED BY PHENOLAX. RECURRENT MACULAR ANNULAR SYPHILID? PITYRIASIS ROSEA?). Presented by DR. H. E. MICHELSON, Minneapolis.

A woman, aged 28, had been under treatment for syphilis for two and a half years before presentation. She had been resting for several months, and at the

time of presentation the Wassermann reaction gave negative results in three tests. Two months previously she noticed an oval lesion on the biceps area of the left arm and a similar lesion on the chest. A friend advised taking cathartics, and the patient used Ex-Lax. Shortly after the ingestion of the drug she noticed a more or less generalized bluish-red macular eruption over the arms and on the trunk. There was a slight scale on some of the lesions and over the back the lesions followed lines of cleavage. However, over the abdomen there were distinct annular lesions without scaling. There were no subjective symptoms.

DISCUSSION

DR. JOHN ARMSTRONG, St. Paul: I should like to ask if any of the members ever saw the lesions of syphilis make perfect rings?

DR. H. E. MICHELSON: I believe that this girl has pityriasis rosea, but the picture is complicated. My procedure will be to do a biopsy, which may throw some light on the nature of the eruption. In answer to Dr. Armstrong's question, I have seen a few cases of the macular annular recurrent neurosyphilid of Unna. This type of eruption often makes perfect, deep red rings without change in the surface. This eruption should always be regarded as an example of recidivation; it usually occurs in patients who have had previous treatment. The macular recurring eruption is resistant, but will disappear with persistent treatment. Dr. Sweitzer and Dr. Winer will recall the case of macular annular recidivation that I showed them last fall. I first saw the patient in that case a year ago. At that time he presented a primary lesion and a papular eruption. In the third month of treatment, an iritis developed and in the tenth month of treatment, the macular annular recidivation appeared. Under treatment with tryparsamide this eruption gradually subsided, but it required four months of active treatment.

DR. J. F. MADDEN, St. Paul: I saw this patient at the outpatient department of the University Hospital about two weeks ago. At that time she had only two lesions, one on the thorax and one on the arm. We considered the possibility of mother plaques of pityriasis rosea. I feel that the ingestion of the drug containing phenolphthalein happened to occur coincidentally between the appearance of the mother plaques and the general showering down of secondary lesions of pityriasis rosea. In view of all the antisyphilitic therapy that the patient has had and the response that she has made, I do not think that the possible presence of syphilis need be considered. The individual lesions favor a diagnosis of pityriasis rosea; most of them are oval with the long axis in the lines of cleavage of the skin; they are superficial; they present a peripheral pink scaling border and a fawn-colored center, and they appeared about two weeks after the appearance of the mother plaques. A diagnosis of pityriasis rosea is preferable.

DR. S. E. SWEITZER, Minneapolis: I agree with Dr. Madden. The patient has had good antisyphilitic treatment, and I see no reason why she should have such a recurrence. Some of the lesions do not look like syphilitic lesions. A diagnosis of pityriasis rosea seems preferable. Persons with syphilis sometimes have other eruptions of the skin. Such an occurrence might explain the peculiar appearance of the lesions on this patient.

DR. L. A. BRUNSTING, Rochester: The appearance of a papular eruption in a patient who is receiving treatment for syphilis brings up a differential problem involving dermatitis medicamentosa (arsphenamine), recurrent syphilid or intercurrent pityriasis rosea, in the order named. Several of the lesions over the shoulders are urticarial wheals that are aggravated by friction. In the event of further therapy for syphilis, arsphenamine should be administered guardedly.

A CASE FOR DIAGNOSIS (PSORIASIS?). Presented by DR. F. W. LYNCH, Minneapolis.

F. G., a white woman, aged 22, from Dr. S. E. Sweitzer's service at General Hospital, presented an eruption on the thigh and the shoulder. She contracted

syphilis in March, 1930, and began treatment in April. She had three courses of bismuth and three of neoarsphenamine. The Wassermann reaction of the blood gave negative results after the first course. Papular scaling lesions were present on the thigh and the shoulder. Biopsy showed psoriasis.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: The microscopic picture is typical for psoriasis.

PSORIASIS. Presented by DR. H. E. MICHELSON, Minneapolis.

A man, aged 38, received a severe injury to the arm and the hand several months before presentation and shortly after this occurrence a generalized papular eruption developed that extended over the entire body. The lesions were papules, each bearing a minute scale and varying in size from that of a pinpoint to that of a pea. The microscopic picture was typical for psoriasis. The Wassermann reaction gave negative results.

DISCUSSION

DR. H. E. MICHELSON: This is a generalized guttate psoriasis of the xanthomatous type.

DR. E. C. GAGER, St. Paul: I think that there may be some relation between the injury and the eruption of the skin. It is a matter of common knowledge that psoriasis has followed vaccination. I should think that psoriasis might follow any injury, particularly if there is any secondary infection, such as some lesion of the capillary body. I think that it might be well to call the attention of the society to the probable necessity of a little attention to the possible occurrence of psoriasis after injury. Some weeks ago I was consulted by an insurance company in the case of a barber who had cut his hand and who had an *Epidermophyton* infection after the superficial laceration of the hand. I do not know whether *Epidermophyton* infection can follow injury, but it is certainly a point well worth considering. From a legal standpoint it is sometimes important to establish the relationship of these eruptions.

ACUTE PSORIASIS. Presented by DR. F. W. LYNCH, Minneapolis.

E. P., a white woman, aged 46, from Dr. S. E. Sweitzer's service at General Hospital, presented an eruption on the trunk. She had an attack of influenza late in December, 1930, with pains in the joints, chills, headache and general malaise. About Jan. 1, 1931, an eruption developed about the waist and the chest. This was accompanied by severe itching, and the condition rapidly became generalized over the neck, chest, abdomen and back, and to a lesser degree on the arms and the legs. There was some scaling. Mild local therapy, consisting of two exposures to the ultraviolet lamp and autohemotherapy, was administered.

Examination showed a dry, scaling, papular eruption with a dully erythematous base, especially marked on the trunk and involving the extremities. Biopsy of one of the lesions showed definite psoriasis.

LINGUA GEOGRAPHICA. Presented by DR. L. H. WINER, Minneapolis.

A. J., girl, aged 7, from Dr. S. E. Sweitzer's service at General Hospital, presented an erythematous lesion on the tongue. Lesions had been present on the anterior third of the left half of the tongue for two years before presentation. On Jan. 10, 1931, the patient came to the Minneapolis General Hospital with multiple, whitish irregular elevated plaques on that area. The area was treated with a one-quarter skin unit dose of x-rays, and the lesions disappeared.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: The patient had a definitely geographic tongue and she still presents that condition to a slight degree. It is difficult to use roentgen rays on the tongue, but the patient showed a good response to them on the anterior portion. Howard Fox stated in a recent number of the ARCHIVES (Fox, Howard: Lingua Geographica Treated by Roentgen Rays, ARCH. DERMAT. & SYPH. **22**:1124 [Dec.] 1930) that he had used roentgen therapy in several cases. An excellent result was obtained in this case as far as the roentgen rays could be applied.

DR. H. G. IRVINE, Minneapolis: I recall having seen a case with Dr. Ormsby about eight or ten years ago, and he suggested the use of radium in cases in which there are only two or three small plaques, and said that he had used it with success. I have treated two or three patients who had lingua geographica; one later went to Portland and Dr. Kingery treated her there. I saw the patient the last time that I was out there, and the result was good. I attempted to treat a university student with x-rays in a case in which the use of radium was out of the question, but he did not return, so I did not see the result. I think that the use of radium was first suggested by Ormsby about eight or ten years ago.

PSEUDOPELADE OF BROCQ. Presented by DR. L. H. WINER, Minneapolis.

R. G., a white woman, aged 66, from Dr. S. E. Sweitzer's service at General Hospital, presented a lesion on the scalp. The lesion was first noticed in 1925 on the occipital part of the scalp and it had progressed until it involved most of the occipital and parietal regions. It was accompanied by itching. No lesions had been noted previously on the scalp.

Examination showed a large atrophic scar involving the occipital and parietal regions of the scalp, about 20 cm. in diameter, and accompanied by alopecia of the area involved. There was no ulceration or any sign of active inflammation.

Biopsy showed marked atrophy of the epidermis. The papillary bodies showed a definite homogenization. The rete pegs of the epidermis were flattened and the hair follicles were absent. The stained section of elastic tissue showed a loss of elastic tissue in the papillary bodies.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I made a diagnosis of pseudopelade of Brocq, but there is the question of scars from favus. The patient gave a history of this disease starting four years before presentation. There was no sign of any active lesions, and biopsy showed atrophy, so with the history of the disease of four years' duration I considered pseudopelade of Brocq the most probable diagnosis.

SUPERFICIAL EPITHELIOMATOSIS. Presented by DR. H. E. MICHELSON, Minneapolis.

A woman, aged 52, had a lesion on the tip of the left shoulder about 3 cm. in diameter. The lesion was deep red and sharply demarcated, and the border was somewhat elevated. In the center there was some degree of atrophy. The microscopic picture was similar to that described by Professor Jadassohn as intraepithelial epitheliomatosis. Roentgen rays will be used in the treatment.

EPITHELIOMA. Presented by DR. JOHN F. MADDEN, St. Paul, for DR. H. E. MICHELSON.

P. B., a man, aged 65, a laborer noticed a "wart" on his back about fifteen years before presentation. This lesion became ulcerated three years thereafter and gradually grew to the size at presentation. The patient presented an ulcer, about 6 by 2 inches (15.24 by 5 cm.), extending along the vertebral column

between the scapulae. The border was rolled, everted and pearly. The ulcer was from about ½ to ¾ of an inch (1.27 to 1.91 cm.) deep. The base presented an unhealthy granulation tissue covered by a purulent exudate. The patient had had no therapy other than "faith healing."

DISCUSSION

DR. J. F. MADDEN: We are not sure that this is a basal cell epithelioma at this time, although a biopsy done a year ago showed a formation that was definitely of the basal cell type. During the past year the ulcer has increased by half in size.

DR. H. E. MICHELSON, Minneapolis: This is an extensive ulceration, and although the section last year showed basal cell epithelioma we are going to take another section from the border for a biopsy and also one from the base, for the base showed only granulation tissue and the border still shows basal cell epithelioma. The treatment will be wide excision with cautery, with subsequent grafts implanted according to the method used by Dr. Rusten.

SYMMETRICAL TELANGIECTASIA OF THE UPPER AND LOWER EXTREMITIES. Presented by DR. L. H. WINER, Minneapolis.

P. B., a white woman, aged 46, from Dr. S. E. Sweitzer's service at General Hospital, presented an eruption on the hands and the arms. A somewhat similar eruption had been present in childhood following exposure to the cold. Since November, 1930, she had noticed that her extremities became cold easily and that a reddish and bluish eruption was evident. This was accentuated on exposure to cold, on contact with water and when her arms were dependent. She had been taking thyroid extract for one month. The condition of the lower extremities had improved.

Examination showed a reticular eruption varying from an erythematous to a cyanotic condition, and becoming more marked distally on the upper extremity. The hands were cold and cyanotic. The eruption became less evident when the arms were elevated.

A specimen of tissue taken from the left forearm for a biopsy showed marked vascular telangiectasis in the stratum papillaris and the upper reticularis.

DISCUSSION

DR. C. A. BOREEN, Minneapolis: I disagree. I think that the condition is due to a circulatory disturbance; it all disappears when the patient raises her arm.

DR. L. A. BRUNSTING, Rochester: The microscopic sections showed numerous telangiectases in the upper cutis without inflammatory reaction. That these are venous spaces is shown quite clearly by the blanching that occurs when the hand is elevated above the level of the heart. It might be interesting to make capillary studies of the nail-beds by the Lombard technic, as well as to estimate the circulatory efficiency of the lower extremities through the use of histamine.

DR. S. E. SWEITZER, Minneapolis: The condition of the legs was as poor as that of the hands. I do not know why the legs responded to treatment with thyroid more than the arms did. We did an early biopsy that was not deep enough to show anything; a later one showed definite vascular changes. The condition of the hands is about the same. It is a peculiar circulatory disease.

DR. H. E. MICHELSON, Minneapolis: I saw the section from this patient before I saw the clinical case, and I judged from the section that we were dealing with a telangiectasia rather than with a livedo. The microscopic picture resembled the one that I exhibited last year from a woman who developed a great number of small cobwebby, nevus-like telangiectasias during the fifth month of pregnancy. These lesions all disappeared at the termination of pregnancy.

SYPHILIS WITH AN ERUPTION RESEMBLING ACNE VARIOLIFORMIS. Presented by DR. L. H. WINER, Minneapolis.

E. A., a white man, aged 40, from Dr. S. E. Sweitzer's service at General Hospital, presented an eruption confined to the forehead. An eruption on the occipital region of the scalp was noticed about 1919. This gradually progressed, and in 1929, it moved forward and was evident at the hair-line in front. There were never more than a few lesions present at any one time.

Examination showed an eruption confined to the region above the right eyebrow, composed of a few somewhat erythematous papules, varying in size from that of a pinhead to that of a match-head. There were numerous scars of a similar size extending up and into the scalp. The Wassermann reaction of the blood was positive.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: The question in my mind was whether the patient had acne varioliformis. We intend to do a biopsy, and a report will be made later. The patient surely has syphilis, and the scars present around the hair-line look like those in acne varioliformis.

FIBROID SYPHILOMAS. Presented by DR. F. W. LYNCH, Minneapolis.

A. K., a colored man, aged 50, from Dr. S. E. Sweitzer's service at General Hospital, presented several enlargements in the soft tissue near the elbows. They had been present for about eighteen years and had not increased in size for the past five years or more. There was no pain or tenderness. A similar mass was removed from the left arm in December, 1930.

Examination showed two subcutaneous, firm, painless nodes on the extensor surface near the right elbow. They were 1 inch (2.5 cm.) and ½ inch (1.27 cm.), respectively, in diameter. An adjacent periostitis was noted.

The Wassermann reaction of the blood was positive and the Kahn reaction was 4+ in November, 1930. The patient had been receiving antisyphilitic therapy since that time.

Biopsy done by removing a tumor from the right elbow showed a dense fibrotic tumor with nests of round cells paravascularly situated; this picture is typical of syphilis of the fibroid type.

DISCUSSION

DR. L. A. BRUNSTING, Rochester: These appear to be definitely "nodosités juxta-articulaires," both clinically and histologically. In 1926, Max Jessner summarized the literature from the time of the first descriptions by Jeanselme. Many of these cases have been reported under other names such as "syphilitic fibromas of the tendon sheaths" or "fibroid gummas." Most of the cases in which syphilis has been proved to be a factor have been reported only as recently as the last decade. The nodules are seen most often over the prominences of the elbows and knees, but they frequently appear as small tumors along the tendon sheaths of the palms and fingers. In 1930, Jessner stated that these nodes were not uncommon among the peasants of Russia.

The histologic picture is not always specific. There may be a dense fibrosis with practically no vascularity or cellular infiltrate; quite frequently at a later stage there is central softening with deposits of calcium and cholesterol. The response of the tumors to antisyphilitic therapy is apt to be slow, especially in cases in which there is much fibrosis.

DR. J. F. MADDEN, St. Paul: A similar case was reported at the last meeting; the patient is now doing well under therapy. Most of the lesions have involuted; others are decreasing in size. Dr. Michelson taught us that the more cellular the lesion, the sooner it responds to therapy. The case previously reported was predominantly cellular.

PRIMARY SYPHILIS IN THE PRESENCE OF CONGENITAL HEMOLYTIC ICTERUS. Presented by DR. F. W. LYNCH, Minneapolis.

J. R., a white man, from Dr. S. E. Sweitzer's service at General Hospital, presented himself at the Minneapolis General Hospital showing a chancre and jaundice evident on the face and the conjunctivae. The jaundice had been present for several weeks, and he had noticed it several times in past years. Examination showed a mild icterus of the face and the conjunctivae, a slightly enlarged liver and a markedly enlarged spleen. Dark-field examination of the penile lesion was positive for *Spirochæta pallida*. Examination of the stool and the urine showed bile pigments in increased amounts. The van den Bergh test was positive, with a direct delayed reaction. The function of the liver was normal. The icterus index was 24 units. Fragility tests with saline solutions showed increased fragility of the red blood cells; 20 per cent of the red blood cells were microcytes.

Treatment had been given with neoarsphenamine and had not been accompanied by any toxic signs or symptoms. The patient was presented as having a case of icterus in which treatment with arsenicals might safely be administered.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: The jaundice has nearly disappeared. We were doubtful as to whether we should give the patient neoarsphenamine; but he has had several doses and is improved. He still has the large spleen, and Dr. Fahr said that he is going to have that removed.

PITTSBURGH DERMATOLOGICAL SOCIETY

JAMES H. FISCUS, M.D., *Secretary*

Regular Meeting, Feb. 19, 1931

LOUIS WILLARD, M.D., *President, in the Chair*

TERTIARY SYPHILIS. Presented by DR. LESTER HOLLANDER.

T. S., a man, aged 35, married, presented a disseminated eruption on the forehead. It was composed of small papules, scars and pigments, and gave the appearance of folliculitis. On the nose the eruption was yellowish and nodular; it affected the anterior nares, extending down and involving the entire upper lip. When it first appeared the condition resembled lupus vulgaris.

On the arm, the trunk and the legs the lesions were dark red with circinate borders. Atrophy was also noted. The neck presented pigmentation (leukoderma colli). The Wassermann and the Kahn reactions of the blood were four plus. The patient was presented on account of extensive cutaneous manifestations of tertiary syphilis.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I agree with the diagnosis of a typical nodular syphilid of the face, but would like to call attention to the unusual irregular outline of two involuted lesions on the patient's shoulder. These had much the appearance of superficial epitheliomas of the types seen in general epitheliomatosis.

DR. LESTER HOLLANDER: I wanted to show the pigmentary changes present and the large variety of lesions.

PAPULONECROTIC TUBERCULID WITH TUBERCULOUS CERVICAL ADENOPATHY. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

L. V., a Negress, aged 31, was first seen three weeks prior to presentation with many firm, deeply pigmented, papular lesions, largely confined to the extensor surfaces of the arms and the legs. Many of these lesions had an inspissated horny central plug. The more active lesions were slightly tender on pressure. Many hyperpigmented depressed scars of old lesions were seen on the same areas as the active lesions. The general physical examination gave negative results except for a group of large confluent glands in the left cervical region. The gynecological and genito-urinary examinations and urinalysis also gave negative results. The Wassermann and the Kahn reactions of the blood were negative.

When the patient was presented the eruption had gradually subsided. This improvement was ascribed to the following factors: the use of cod liver oil internally, local medication and deep roentgen therapy to the tuberculous glands.

DISCUSSION

DR. LESTER HOLLANDER: I want to ask Dr. Busman whether the treatment is that recommended by Dr. Goeckerman. I would advise a gastro-intestinal study.

DR. A. R. WOODBURNE: The lesions of the skin and the glands of the neck have both improved at least 50 per cent following deep therapy to the glands of the neck and systemic tonic medication. In view of the definite lesions present showing allergy to tuberculosis (cervical adenopathy), I believe that it is not necessary in this case to consider the question of enteroptosis.

MOLLUSCUM FIBROSUM. Presented by DR. B. A. GOLDMANN.

M. G., a white girl, aged 15, from the dispensary of the University of Pittsburgh, presented a tumor the size of a hazelnut over the left angle of the mandible. The growth began four years previous to presentation following an injury to the chin. The mass was a soft flabby growth. On palpation no fluctuation of pulsation could be elicited. Over the remainder of the body the patient presented numerous small, pinkish, soft tumor masses and numerous brown pigmented nevi. Scoliosis of the spinal column was present. The patient stated that a similar condition existed in a greater degree in her father, uncle and aunt.

VON RECKLINGHAUSEN'S DISEASE. Presented by DR. W. H. GUY and DR. F. M. JACOB.

A white girl, aged 18, presented numerous soft nodules and pigmentary lesions chiefly on the trunk. One large lesion had been removed surgically from the left cheek several years previously. The father had a similar condition.

DISCUSSION

DR. B. A. GOLDMANN: Cannot some of these lesions be removed surgically?

DR. W. H. GUY: Since the question of surgery has been raised, it may be wise to call attention to the fact that these cases are frequently poor surgical risks.

KERATOSIS PALMARIS HEREDITARIA. Presented by DR. FREDERICK AMSHELL.

J. M., a woman, aged 44, was seen on March 20, 1931, at the dispensary of the Montefiore Hospital. She presented a symmetrical eruption on both palms. The horny layer of the skin was dark brown and greatly thickened with exaggeration of the natural surface lines. There were no signs of inflammation and the patient complained only of the appearance. The condition had been present since birth. Her father and a brother had a similar condition. Of six children in the

family the patient and a brother were affected. The brother had two children and one of them, a boy, was affected. In addition, the patient had a leukoderma of twenty years' duration.

LICHEN PLANUS BULLOSUM. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

J. H., a woman, married, aged 32, white, an American, was first seen on Feb. 26, 1931, with generalized papular and annular lichen planus of the trunk and the extremities of three months' duration. The condition was extensive and practically solid over the entire trunk and the extremities. The face was free from the condition and there were no visible lesions in the mucous membrane. There was mild pruritis, but there were no constitutional symptoms. The general physical examination gave negative results. Treatment was instituted consisting of fractional doses of unfiltered roentgen rays, neoarsphenamine administered intravenously and corrosive sublimate internally. A week after the first visit a few small vesicles were noticed on the extremities and on subsequent visits the general picture of lichen planus had subsided; there was, however, diffuse erythema of the arms and the legs with the formation of multiple vesicles and bullae.

DISCUSSION

DR. LESTER HOLLANDER: I believe that the bullous lesions are produced artificially. Duhring's disease must be considered however.

DR. H. G. WERTHEIMER: I recall a similar case which I saw years ago. At first it was a typical case of lichen planus in which arsenic and bichloride of mercury were given together with tar baths. Within a short time a vesicular and bullous eruption appeared, so that in the course of time the entire body was covered with a pemphigus-like eruption, the lichen lesions having entirely disappeared. When the bullous eruption subsided, the lesions of lichen planus reappeared, but this time in the annular form. I have often wondered what part, if any, the medication had in the bullous eruption.

DR. B. A. GOLDMANN: This patient also has bullous lesions about the neck which are on a noninflammatory base. I feel that this is a case of dermatitis herpetiformis.

DR. JOSEPH ELLER, New York: I believe that this is a case of Duhring's disease. There is a great deal of pigmentation with groups of vesicles and bullae on the upper part of the chest and back especially. There is also diffuse dermatitis with areas 6 and 7 inches (15 and 17 cm.) in length. The patient gave no history that she had been applying salves other than that given by the presenter, and the one used was more or less emollient.

DR. UDO J. WILE, Ann Arbor, Mich.: I believe that if Dr. Busman had not seen the case at a time when the lichen planus was clinically identifiable, he would be inclined to regard the case as one of dermatitis herpetiformis.

CARCINOMA (BASAL CELL TYPE). Presented by DR. LESTER HOLLANDER.

H. T. a Negro, aged 31, presented a large ulcerative area involving the anterior wall of the chest. Ten months previously this patient was burned and the present condition developed slowly since then.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: Carcinomas following burns are usually of the prickle-cell type.

DR. JOSEPH ELLER, New York: I agree with Dr. Wile. Basal cell carcinoma following a burn is unusual.

BLASTOMYCOSIS. Presented by DR. LESTER HOLLANDER.

J. J. H., aged 32, a colored man, presented a fairly well generalized, disseminated eruption. Each individual group of lesions appeared as a verrucose, oval patch with central depression. The treatment consisted of large doses of iodide.

MILIARY LUPUS RESEMBLING ROSACEA. Presented by DR. W. H. GUY and DR. F. M. JACOB.

A woman, aged 37, presented an eruption of one year's duration, limited to the center of the face. The appearance except on close inspection resembled rosacea. The individual lesions comprised soft brownish-yellow tubercles the size of a pinhead, showing histologically a tuberculous structure. General examination failed to disclose tuberculosis elsewhere in the body.

TUBERCULOSIS LUPOSA. Presented by DR. LESTER HOLLANDER.

Mrs. S. M., aged 39, presented an eruption which affected the face and the hands. There were three lesions on the face which were dusky red and presented numerous areas of telangiecta sia. Diascopic pressure showed brownish discoloration and there were yellowish, apple jelly-like nodules within the lesion. The interesting feature was presented on the fingers. The distal phalanges of all the fingers were involved. They had a cat-o-nine-tail appearance. The lesions on the fingers were of solid consistency. Roentgenologic examination showed a spongy character of the terminal phalanges. The general examination for pulmonary tuberculosis gave negative results, but the roentgenologic study showed that there was a rather diffuse infiltration in both pulmonic fields limited almost entirely to the hilus and the median zones, which was suggestive of old bronchitis with possible bronchiectasis. The tonsils and the infected teeth had been removed. The blood picture showed: white blood cells, 2,800; red blood cells, 4,000,000; hemoglobin, 66 per cent; color index, 0.82. Serologic examination gave negative results. Roentgenograms of the hands were shown.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I believe that this was a most unusual and interesting case and an example of typical sarcoid tuberculosis with a tuberculoma involving the finger-tips and tuberculous changes in the bones of the fingers. I am under the impression that a case of sarcoid with changes in the bone similar to these was shown and was reported in the proceedings of the Chicago Dermatological Society; I cannot recall by whom the case was presented.

DR. W. H. GUY: The case was of interest in that the lesion on the forehead strongly suggested sarcoid associated with rarefaction of bone of the distal phalanges, underlying granulomatous infiltrations of long duration and the suggestive observations in the chest. The relationship of sarcoid and changes in the bone was of particular interest. I think that the entire process is tuberculous.

DR. G. J. BUSMAN: We had a case like this at the Mayo Clinic. A young woman had lesions on the fingers and the toes with changes in the bone and also lesions on the face which we diagnosed by section as sarcoid of Boeck. The lesions responded nicely to treatment with neoarsphenamine.

DR. LESTER HOLLANDER: It is interesting to see lesions affecting the hands and the feet. I want to call attention to the roentgenograms which show the resorption of the lesions of the bone.

GRANULOMA INGUINALE OF THE GLANS PENIS. Presented by DR. G. J. BUSMAN and DR. A. R. WOODBURNE.

S. W., colored, aged 27, was first seen five weeks ago with a deeply extending, destructive, slowly advancing ulcer of the glans penis. He had been formerly

treated for ulcus molle for nine or ten months at several of the local clinics. The borders of the ulcer were firm but not pearly, and were only mildly inflammatory. The edges were overhanging and ragged, and the base was dirty and covered by a thick grayish pus. The Wassermann and the Kahn tests both gave negative results. A smear showed bodies that were suggestive of the Donovan bodies seen in granuloma inguinale. The biopsy showed a small ulcer with slightly edematous epidermis on either side. The base was filled with a large mass of small polymorphonuclears in which no organism could be demonstrated in the tissue section. Deep in the subcutaneous tissue were many islands of polymorphonuclear and mononuclear lymphocytic infiltrations. There was definite edema of the endothelium and endarteritis of the small vessels in many places associated with a periarteritis of marked degree. The fibrous tissue was compact and there was some destruction of the collagen. A polymorphonuclear giant cell of the foreign body type was seen.

The general physical examination gave negative results as did urinalysis. There was no enlargement of the inguinal glands. When the patient was presented there had been a marked improvement with healing of almost 50 per cent in the past four weeks after about six injections of 1 cc. of a 5 per cent solution of tartar emetic.

DISCUSSION

DR. LESTER HOLLANDER: I have a number of proved cases of granuloma inguinale which did not improve on tartar emetic.

DR. W. H. GUY: I feel that Dr. Wile's cases, one of which I have seen, were of a different type from granuloma inguinale in which tissue smears reveal Donovan bodies in large mononuclears. In the majority of the latter cases tartar emetic is effective.

CLEVELAND DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Feb. 26, 1931

J. R. DRIVER, M.D., *Presiding*

PSEUDO-ACHROMIA PARASITARIA. Presented by DR. R. E. BARNEY.

J. M., a white girl, aged 16, stated that in June, 1930, she had noticed pruritic, brown, scaling patches on the trunk. Three months later she had taken sun-baths, following which the brown spots had disappeared, leaving white areas. There was extensive depigmentation over the chest and back. The borders of these areas were convoluted, suggesting the confluence of smaller original lesions, and there were outlying satellites, varying in size from that of a large pinhead to that of a medium-sized coin. There was no scaling or inflammation, and repeated examination of scrapings revealed neither spores or hyphae.

DISCUSSION

DR. H. N. COLE: This condition was described recently in the *Annales de dermatologie et de syphiligraphie*. Following treatment, the brown scaly spots leave pseudo-achromic areas.

DR. R. E. BARNEY: It was described by Kistiakowsky in the December, 1930, issue of the *Annales*, under the title given for this case. The author expressed the belief that the scales and fungus of tinea versicolor filter out the rays when the patient is exposed to the sun or the ultraviolet lamp, leaving areas that are lighter in color than the surrounding pigmented skin. The fungus can be demonstrated

before treatment, and finally, when only the pseudo-achromic areas remain, no fungus can be found.

CASES FOR DIAGNOSIS (LICHEN PLANUS ATROPHICUS?). Presented by DR. R. E. BARNEY.

S. V., a laborer, aged 37, had been presented before the Society in December, 1930, with a diagnosis of lichen planus atrophicus. At that time the eruption had been present for six weeks. Since then the condition had improved, the treatment having consisted of arsenic by mouth and stimulating local applications. During this interval the patient's wife and two children were found to present lesions of a similar character.

A son, aged 4, had had the eruption for about four months. In the midline of the lower part of the back there was a small, coin-sized, purplish, depressed, slightly infiltrated, sharply marginated lesion. On the upper half of the right buttock there were shiny, white, angular, flat, umbilicated papules the size of a pinhead. There were several large pinhead-sized atrophic lesions at the junction of the upper and middle thirds of the right thigh.

Further study of the eruption in the father and examination of the wife and two children threw doubt on the original diagnosis of lichen planus atrophicus.

DISCUSSION

DR. J. E. FISHER: I believe that the son has lichen planus and the father lichen planus atrophicus.

DR. H. N. COLE: The father's grouped lesions suggest an old syphiloderm.

DR. E. W. NETHERTON: I do not believe that these are cases of lichen planus atrophicus. The grouping of the father's lesions is not as extensive as one usually sees in late syphilis.

DR. R. E. BARNEY: I believe that these patients do not have lichen planus atrophicus, although I cannot make a definite diagnosis. In the father, the process seems to begin as large or small, flat, angular, umbilicated white papules the size of a pinhead, which enlarge, form slightly depressed, ringed lesions and later become purplish.

SYPHILITIC ONYCHIA (?). Presented by DR. R. E. BARNEY.

Mrs. L. R., aged 24, presented a deformity of all of the nails, of five months' duration, the right middle finger having been affected first. The distal half of every nail was elevated from its bed. There were hard, hyperkeratotic masses beneath some of the nails, but most of the nail-beds were apparently normal. The nail plates were brittle, but not thinned, pitted or striated. There was no paronychia, and none of the distal phalanges were clinically involved. Roentgen studies revealed no bony change in the fingers. No spores or mycelium had been found after repeated examination of the hyperkeratotic masses beneath the nail plates. The Wassermann reaction was positive.

DISCUSSION

DR. M. J. GIBANS: Some of these cases are supposedly of neurotrophic origin.

DR. C. L. BASKIN: I have seen several similar cases in persons who, in manufacturing hot water bottles, have their hands immersed in water to which some alkali has been added.

DR. J. E. RAUSCHKOLB: I agree with the diagnosis as presented. There is atrophy at the free border of the nails and a shortening of the nail plates, producing the so-called spade nails.

DR. H. N. COLE: I agree with Dr. Baskin. The fact that only the finger-nails are involved speaks against syphilis. I have seen similar cases in patients working with alkalis.

ERYTHEMA MULTIFORME. Presented by DR. H. F. DEWOLF.

W. S., a boy, aged 17, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, presented an extensive vesicular, eroded involvement of the entire mouth and throat, with some fever and marked tenderness, of six days' duration. The tonsils were enlarged and infected. There had been similar attacks four and two years, respectively, before the time of presentation. An occasional Vincent's organism had been found in the dark-field examination of specimens. The Wassermann reaction was negative.

DISCUSSION

DR. EMERSON GILLESPIE: From the history of recurrent attacks and the fact that the present eruption is limited to the mouth, I believe this to be a case of erythema multiforme. There is no history of the ingestion of drugs. Even though a few Vincent's organisms were found in the lesions, they are probably of no significance.

DR. J. R. DRIVER: Clinically, this is a case of erythema multiforme.

ACRODERMATITIS PERSTANS. Presented by DR. H. F. DEWOLF.

I. G., a girl, aged 5, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, who had been presented at the January, 1931, meeting of the Society, had had an exacerbation of the eruption on the hands and feet since that time. Some improvement had followed the use of applications of methyl violet.

LYMPHOSARCOMA (?); HODGKIN'S DISEASE. Presented by DR. H. F. DEWOLF.

S. V., a boy, aged 19, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had first noticed large glands in the left side of his neck four and one-half years before presentation. A gland had been removed, and a pathologist had made a diagnosis of lymphosarcoma. At the time of presentation, there was a large ulcerative process the size of the palm, of seven months' duration, at the right side of the neck, and both sides of the neck were swollen. There was diffuse edema of the face and neck, and the eyelids were practically swollen shut. There was also edema of the right upper extremity. All of the superficial lymph nodes were enlarged, especially those in the axillae. The skin was dry, with many crusted excoriations. Severe pruritus had been present for two or three months. Examination of the blood revealed: erythrocytes, 5,200,000; hemoglobin, 70 per cent, and leukocytes, 44,000; the differential count showed: neutrophilic polymorphonuclears, 92 per cent; small mononuclears, 2 per cent; large mononuclears, 2 per cent; transitionals, 3 per cent, and eosinophils, 1 per cent. Roentgen studies of the bones revealed no abnormality, while the mediastinal and peritracheal lymph nodes in the chest were found to be enlarged. Biopsy of the skin revealed nothing. No lymph node had been removed.

LYMPHANGIOMA OF THE BUTTOCK. Presented by DR. H. F. DEWOLF.

S. S., a man, aged 25, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had been presented before the Society at the meetings of November, 1930, and January, 1931. He was presented again to show the great improvement following intensive treatment with radium, which was described at the presentation in January. The mass had greatly diminished in size, practically the entire papillomatous surface had disappeared, and the treated area was healing uneventfully. This was in marked contrast to the untreated lower portion of the tumor, which presented its original appearance.

DERMATITIS VENENATA DUE TO THE APPLICATION OF ADHESIVE PLASTER. Presented by DR. H. F. DEWOLF.

J. P., a man, aged 52, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had received an injury to the chest in January, 1931; adhesive plaster had been applied, and a severe dermatitis resulted. The dermatitis had been limited sharply to the areas that had been covered by the tape. A patch test with zinc oxide adhesive plaster gave positive results within twenty-four hours, and one with orris root gave positive results after twenty-four hours.

DISCUSSION

DR. J. V. VAN CLEVE: A patch test with adhesive plaster gave a positive reaction within twenty-four hours. We learned that the plaster contained orris root, and so a test was made with a 1:3 mixture of orris root and petrolatum. The reaction to this test was negative in twenty-four hours, but after seventy-two hours there was a definitely positive reaction. A patch test with orris root mixed with water gave positive results in twenty-four hours, while patch tests with zinc oxide and boric acid gave a negative reaction. Therefore, we believe that orris root was the irritant in the adhesive plaster.

DR. J. R. DRIVER: Hitherto we had always considered zinc oxide to be the offending substance, but in this case it is probably orris root.

DR. H. G. MISKJIAN: Adhesive plaster often produces a mechanical irritation which may become secondarily infected. In the present case, however, the dermatitis is apparently chemical in origin.

DERMATITIS FACTITIA. Presented by DR. H. F. DEWOLF.

W. McD., a woman, aged 30, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had burned the back of her hand with hot grease four months previously. The burn had healed uneventfully. At the time of presentation, there was a healing dermatitis, of two weeks' duration, at the site of the former burn. The borders of the patch were sharply angular. There had been a vesicular exacerbation, with some extension of the process, several days previously, following the physician's suggestion that the lesion would advance.

DISCUSSION

DR. BENJAMIN LEVINE: I believe this to be a case of dermatitis factitia.

DR. J. E. RAUSCHKOLB: When I first saw the patient, the eruption was of four days' duration. She said that her hand had become red suddenly. The upper border of the eruption was sharply outlined, and there was local heat; my diagnosis then was erysipeloid. More lesions were produced while she was under observation. Later I learned that she had been using a soap containing mercuric iodide. The eruption healed on the fingers, but advanced up the back of the wrist, and its present appearance indicates that it must be factitious.

DR. J. R. DRIVER: It is interesting to know that the lesion began to improve rapidly as soon as hospitalization was advised as necessary.

DR. R. E. BARNEY: The facies of this woman fits in well with the diagnosis of dermatitis factitia.

A CASE FOR DIAGNOSIS (PUSTULAR PSORIASIS?). Presented by DR. H. N. COLE and DR. J. R. DRIVER.

W. R., a man, aged 27, a physician, stated that he had injured his left little finger in 1918, and that "proud flesh" had persisted at this site for three years. In 1922, he had first observed psoriasiform lesions on the elbows and on the extensor surfaces of the legs and thighs. At that time, Dr. W. H. Guy had presented him at a meeting of the Pittsburgh Dermatological Society. Anti-

syphilitic treatment was recommended, but it was employed without benefit. Later, in 1923, the condition healed completely under local applications, and there were no further manifestations until 1926. Since 1926 there had been four recurrences, with the skin practically clear between the attacks. All of the outbreaks had been similar, consisting of more or less generalized psoriasiform eruptions accompanied by the formation of pustules and changes in the finger-nails. In 1928, during a flare-up of the disorder, vitiligo had appeared on the chest. At no time since 1928 had the finger-nails been entirely free from lesions.

The patient presented a more or less generalized eruption. Over the scalp there were numerous thick and confluent, scaling areas, involving almost the entire hairy portion. There was no loss of hair. Plaques on the elbows showed silvery scales, the removal of which left minute bleeding points. On the trunk there were irregular areas of hyperpigmentation and depigmentation, together with scattered scaling papules, which extended over the thighs and became confluent about the knees. Distributed over the hands, especially over the fingers, and on the toes and legs, there were numerous, confluent, very fine, slightly raised lesions, with a delicate membrane over the surface, which, on removal, revealed a small lake of pus. There was a certain amount of atrophy of the tissues of the fingers and toes, and atrophy of many of the finger-nails, the nail-bed being replaced by these extremely fine, superficial pustules. The remaining nails were stippled, and there was a tendency to thickening and piling up of the substance of the nail at the free border.

The urinary, serologic and hematologic laboratory observations had been normal, including the chemical analysis of the blood. Cultures of the blood yielded *Staphylococcus epidermidis albus*, which was probably a contamination. Cultures from the pustules and finger-nails invariably yielded *Staphylococcus epidermidis aureus*. A biopsy specimen was shown.

DISCUSSION

DR. H. G. MISKJIAN: There are typical lesions of psoriasis on the scalp and arms, and the hyperpigmentation and depigmentation of the trunk may be due to previous treatment with ultraviolet rays. The small subepidermal vesicles and pustules seem characteristic of dermatitis repens. The possibility of mycosis fungoides might be kept in mind, although the sections show nothing indicative of this disease.

DR. J. M. CAVANAUGH: Dr. Guy saw this patient in Pittsburgh, and believed that the disease was dermatitis repens. He also considered the possibility of mycosis fungoides or psoriasis, with a sensitivity to a staphylococcus as a secondary invader.

DR. J. E. FISHER: The condition seems to be psoriasis, possibly changed by previous treatment.

DR. J. R. DRIVER: This patient and the girl shown today with erythema perstans present an interesting problem. The latter entered the hospital with lesions resembling impetigo, and her sister came into the hospital at the same time with typical lesions of impetigo which healed completely in a short time. The girl's lesions, however, were resistant to treatment, involving first the face and hands, and later the feet; they are now characteristic of dermatitis repens. Her lesions are similar to those of this man: tiny superficial vesicles, becoming pustular. I believe that the man also has dermatitis repens.

DR. R. E. BARNEY: This is apparently a case of psoriasis and pyoderma, and the pigmentary changes might be due to previous ultraviolet or roentgen irradiation. The changes in the nails appear to be psoriatic.

DR. H. N. COLE: Our tentative diagnosis has been dermatitis repens complicated by psoriasis. In a recent number of the *British Journal of Dermatology* there is a good deal of discussion regarding acrodermatitis perstans and pustular psoriasis, the authors taking the stand that pustular psoriasis is a distinct entity,

which should be separated from acrodermatitis perstans on the ground that no positive cultures can be found in the former. In our case, cultures showed a staphylococcus, which may have been a contamination. Perhaps this case should be classified as pustular psoriasis, although in many ways it accurately resembles dermatitis repens in its history, course and present appearance.

ACTINOMYCOSIS. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

I. M., a white boy, aged 15, with an irrelevant family and personal history, stated that his cutaneous manifestations had begun four months previous to presentation with the appearance of a small red papule on his back. Following excoriation, it had apparently become infected, for it enlarged and became more painful. Two months before presentation, the lesion had been incised by a physician, but no pus was obtained; at about the same time three other papules were observed. There had been fever, slight loss of strength and the loss of 5 pounds (2.3 Kg.) in weight.

At the level of the ninth rib, just to the right of the vertebral column, there was a mass about as large as an orange. Near its center was an area of soft, moist, bluish-red, granulomatous tissue, from which a considerable quantity of whitish yellow pus exuded. The mass seemed to fluctuate, but no fluid could be obtained by aspiration. A probe could be passed into the granulomatous tissue for several inches in any direction. There was a small papule over the left scapula and one on the left thigh, as well as one on the forearm, which had been removed for histologic examination. They were red, with a scaly crust, beneath which a small amount of pus was found.

The leukocyte count was 14,200, and the erythrocyte count 3,440,000. The Wassermann reaction of the blood was negative. Tuberculin tests gave negative reactions, except in the strength of 1:1,000, which was faintly positive. Cultures from the lesion on the back yielded *Staphylococcus aureus* and *Mastigocladium*. No acid-fast organisms were demonstrated in the smears or in the biopsy sections. Guinea-pigs had been inoculated. A culture of the blood was negative. Roentgen studies of the lungs, spine and ribs showed no involvement of these structures. The pathologist had made a diagnosis of cutaneous tuberculosis from the biopsy specimen, which was presented. (Subsequent cultures have established the diagnosis of actinomycosis, not of the bovine type.)

DISCUSSION

DR. H. G. MISKJIAN: This patient showed several small, grayish, bean-sized papules which might make one think of tuberculosis, but the depth of the large tumor argued against this. There is a possibility of mycosis fungoides, although the section shows no evidence of that condition.

DR. H. N. COLE: When this patient was first seen we considered the possibility of this being a blood-borne type of generalized tuberculosis colliquativa. The large tumor mass, with its anemic, indolent type of granulation tissue was suggestive of this possibility. Careful study of the patient revealed no focus of tuberculosis in the body. The histologic appearance of the tissues might be that of tuberculosis or of several other types of granuloma. We have injected some material from the large tumor into guinea-pigs, but there have been no visible results after four weeks. We have not found tubercle bacilli in the tissues, but we have consistently found *Mastigocladium* in cultures taken from the tumors. We plan to inject specimens of blood into guinea-pigs. Only in the last few days have we found the process to be actinomycosis, although no ray fungus has been found at any time.

CYLINDROMA. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

L. R., a white man, aged 59, had first noticed a wen on his scalp at the age of 6 years. The tumor had gradually grown to the size of a large orange,

until it had been ruptured by an injury on Aug. 11, 1930. It had then become infected, and had been excised on August 26. One month later a swelling had appeared in the scar, and had gradually spread over the entire left side of the scalp and neck. Two roentgen treatments had been administered. For three weeks the patient had been complaining of epigastric pain, nausea and vomiting.

There was a convoluted, diffuse, indurated mass over the left side of the neck and left posterior portion of the scalp, extending down to the supraclavicular region, and anteriorly to the submaxillary region. The entire region of the left trapezius muscle was purplish and showed brawny induration. There were several, pea-sized, ulcerative masses behind the left ear and in the occipital region. In the midline at the superior part of the occiput there was a large scar the size of a coin. The rest of the physical examination gave essentially negative results, except for a visible swelling in the right epigastrium which, on palpation, seemed to be a firm, rounded nodule attached to the liver. A biopsy specimen was shown.

DISCUSSION

DR. H. J. PARKHURST: The clinical and histologic features were those of an endothelioma. In the cases that I have seen previously the growths have all occurred at the front of the scalp rather than posteriorly.

DR. H. N. COLE: The areas seen in the section, surrounded by one or two layers of cells often in the shape of an embryonic gland, were probably areas of hyaline degeneration, which have been described by Darier in connection with the histology of this condition. I consider this a typical example of cylindroma of the scalp. When the patient entered the hospital he had thirty or forty, striking, large, convoluted tumors over the back of the head, most of which have disappeared following the use of radium packs. The history of development of cylindroma from a wen is typical.

HIDRADENOMA OF THE LOWER EYELIDS. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

L. D., a woman, aged 29, had first noticed the appearance of small papules on the lower eyelids five years before presentation. On each lower eyelid there was a cluster of small, flat, yellow-tinged papules. Histologic examination revealed the presence of many minute cysts and epithelial strands or islands within the corium. In many instances these islands were budlike extensions from the preformed glands.

ARTERIAL EMBOLISM FOLLOWING THE INJECTION OF MERCURIC SALICYLATE. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

On Feb. 12, 1931, about twenty minutes after his seventy-first intramuscular injection of mercuric salicylate, the patient had experienced a severe pain in the right buttock. He had had a feeling "as if the mercury was tearing apart the flesh." That night he had observed that the buttock was somewhat swollen and showed an irregular, somewhat reticulated bluish discoloration. A throbbing pain persisted for five days and then subsided as the discoloration began to fade. One week later there was discoloration varying from purplish to bright red in the central part of the buttock, in the shape of a band about 2.5 cm. wide and 10 cm. long, with gyrate borders. There was no local heat or swelling at that time, and gentle palpation caused no discomfort, but active motion was still painful.

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Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: New Orleans. Time: 1932.

American Dermatological Association

W. H. Mook, 3720 Washington Blvd., St. Louis.
W. H. Guy, Secretary, 7026 Jenkins Arcade, Pittsburgh.

British Association of Dermatology and Syphilology (Canadian Branch)

Philip Burnett, President, 2 Simpson St., Montreal.
L. P. Ereaux, Secretary, 1380 Sherbrooke West, Montreal.
Place: Toronto. Time: 1932.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore and Washington Dermatological Society

Isaac R. Pels, President, 1010 St. Paul St., Baltimore.
H. Hanford Hopkins, Secretary, Johns Hopkins Hospital, Baltimore.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
J. W. Bailey, Secretary, 10th St. and Grand Ave., Des Moines, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.
Place: Boston. Time: April 13, 1932.

Southern Medical Association, Section on Dermatology

Chairman: Clifton Brooks Willmott, 608 S. 4th Ave., Louisville, Ky.
Emmet R. Hall, Secretary, 1001 Exchange Bldg., Memphis, Tenn.

STATE DERMATOLOGIC SOCIETIES

Louisiana Dermatological Society

R. A. Oriol, President, 921 Canal St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 150 Baronne St., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Edward R. Maloney, Chairman, 853 7th Ave., New York.
George C. Andrews, Secretary, 115 E. 61st St., New York.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

Sigmund S. Greenbaum, President, 1714 Pine St., Philadelphia.
Stanley Crawford, Secretary, 200, 9th St., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

MINNESOTA DERMATOLOGICAL SOCIETY

C. A. Boreen, President, 920 Medical Arts Bldg., Minneapolis.
D. D. Turnacliff, Secretary, Yeates Bldg., Minneapolis.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

James Stevenson, President, 108 W. 6th St., Tulsa.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

LOCAL DERMATOLOGIC SOCIETIES

ATLANTA DERMATOLOGICAL SOCIETY

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

BRONX DERMATOLOGICAL SOCIETY

Henry Silver, Chairman, 290 West End Ave., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

Abraham Walzer, President, 217 Clifton St., Brooklyn.
A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.

CHICAGO DERMATOLOGICAL SOCIETY

Henry E. Michelson, 80 S. 7th St., Minneapolis.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

H. Jerry Lavender, President, 716 Provident Bank Bldg., Cincinnati.
L. E. Valker, Secretary-Treasurer, 916 Provident Bank Bldg., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

Howard J. Parkhurst, President, 316 Michigan St., Toledo.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

Claud W. Behn, President, 1546 David Whitney Bldg., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.
Place: Cleveland. Time: Nov. 19, 1931.

LOS ANGELES DERMATOLOGICAL SOCIETY

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Chris R. Halloran, Secretary, 1052 W. 6th St., Los Angeles.

Manhattan Dermatologic Society

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Philip Burnett, President, 2 Simpson St., Montreal.
Lemuel P. Ereaux, Secretary-Treasurer, 1390 Sherbrooke St., West, Montreal.

New York Academy of Medicine, Section of Dermatology and Syphilis

Joseph J. Eller, Chairman, 100 W. 59th St., New York.
Leo Spiegel, Secretary, 241 W. 100th St., New York.

New York Dermatological Society

John Frank Fraser, President, 100 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Philadelphia Dermatological Society

Carroll S. Wright, President, 1402 Spruce St., Philadelphia.
Jacques P. Guequierre, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

J. H. Fiscus, Chairman, 121 N. Main St., Greensburg, Pa.
Claude B. Norris, Secretary, 244 Lincoln Ave., Youngstown, Ohio.
Place: Pittsburgh. Time: Spring, 1932.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Howard Morrow, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.